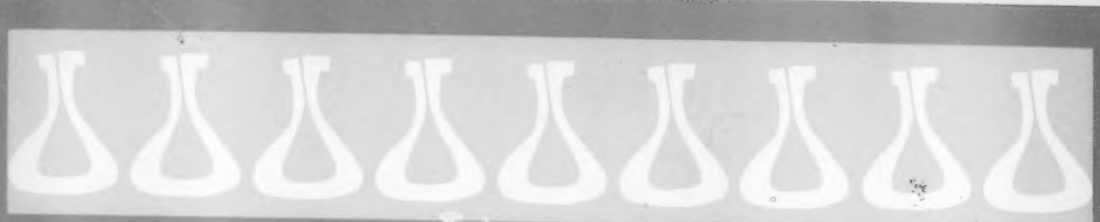

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PSYCHOPHARMACOLOGY ABSTRACTS

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ABSTRACTS

PRECLINICAL PSYCHOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

072412 No author. Author address not given Harnessing potent hallucinogens. *Medical World News.* 11(37):36W, 1970.

Following his synthesis of the antidepressant 2,5-dimethoxy-4,alpha-dimethylphenethylamine (DOM), Dr. Alexander Shulgin is developing compounds that are highly specific for various psychological problems. Phenethylamines seem to affect perception and intellectualization in response to sensory stimulation, while the indoles effect an ego modifying change, and a bromo analog of DOM enhances sensory and emotional responses without sensory distortion. Another mescaline analog (DOET) sharpens perception but does not act on the sympathetic nervous system, and may prove useful both in opening up the patient for psychotherapy and as an antidepressant.

072705 Galzigna, Lauro. Department of Chemistry, University of California, San Diego, Calif. Complexes between acetylcholine and catecholamines and their tolerance to mental illness. *Nature (London).* 225(5237):1058-1059, 1970.

A mixture of Tris-HC1 0.1M pH 7.4and dioxane (1:10) was used with a conductivity of about 3 microSiemens and an Eh value of 185mV to test the chemical interaction between central chemical transmitters and neurotropic drugs, postulated as the chief event responsible for the pharmacodynamic effect of some neurotropic drugs. The study led to the postulation that if a central catecholamine is leaking at any synapse devoid of the enzymatic system that destroys it, the slightly oxidative conditions together with the hydrophobicity of the medium are sufficient to bring about a physiological aminochrome formation, as occurs in the in vitro system. If this takes place at the level of cholinergic synapses, the aminochromes so formed can accumulate and be stabilized by acetylcholine. The leak of catecholamine and the stabilization of its oxidation products would produce an aberrant communication which, on the one hand, might be the chemical event leading to a short circuit between adrenergic and cholinergic systems and, on the other hand, might be the origin of irritative foci of stabilized psychotogenic agents at cortical level. Both effects could possibly explain the onset of mental illness. 10 references.

073265 Voldeng, A. Nelson. author address not given /Synthesis of adamantyl esters./ Terminal report: MH-16720. Final Report, NIMH Grant MH-16720, 1970. 3 p.

A summary of a project which prepared adamantyl esters of known phenazine type phenothiazine tranquilizers is presented. Adamantyl esters of 7 psychoactive compounds were prepared: perphenazine, fluphenazine, clopenthixol, oxazepam, hydroxyzine, pinoxepin, and opipramol. The molecular structure diagrams are included.

074074 Catalfomo, Philip; Eugster, Conrad Hans. School of Pharmacy, Oregon State University, Corvallis, Oregon Amanita muscaria: present understanding of its chemistry. *Bulletin on Narcotics.* 22(4):33-41, 1970.

An outline of the chemical components known to occur in the genus Amanita is presented in this review of the available chemico - pharmacological information on Amanita muscaria and related species. Among the components considered in detail are: ibotenic acid, muscimol, muscazone, muscarine and pigments. Structural formulae and chemical reactions are presented. The present knowledge of the chemistry of Amanita muscaria apparently fails to explain fully the physiological actions stimulated by the ingestion of adequate amounts of the mushroom. It remains to be determined whether or not the total toxicity caused by this mushroom is due to as yet undiscovered substances or if the combined actions of several substances ultimately prove to be the answer. The older literature presents what must now be considered erroneous conclusions with regard to the role played by certain substances in the intoxicating properties of Amanita muscaria. Specific compounds or terms are discussed with regard to this questionable relationship: muscarine, philzatropine, tropane alkaloids and bufotenine. It is hoped that the review and discussion has placed these inconsistencies in proper perspective, and that the inconsistencies will cease to be perpetuated in future literature. In the meantime, work continues that may establish eventually which chemical entities are responsible for the physiological activities of Amanita muscaria. 41 references. (Author abstract modified)

074844 Klemm, Leroy H. University of Oregon, Eugene, Oregon Thienopyridine analogs of serotonin and tryptophan. Final Report, NIMH Grant MH-17304, 1970. 17 p.

Progress in the synthesis of thienopyridine analogs of serotonin and tryptophan is reported. At this point, success has not been attained for all of the synthetic goals sought, but it appears that preparation of 2 thieno/2,3-b/pyridine analogues of tryptamine and 2 of tryptophan should be forthcoming with limited additional work. Time and finances did not allow a start to be made on syntheses of analogs of serotonin and melatonin, although it was proposed in the original application to prepare thienopyridineanalogs of tryptamine, tryptophan, melatonin, and serotonin for use (by others) in biological testing. Key steps in this proposal involved direct chloromethylation and formylation of thieno(2,3-b)pyridine (I) at C-3. However, neither of these reactions could be effected. In an alternative approach a study of direct halogenation of I was made. Results are summarized in scheme 1, where it is noted that the desired 3-bromo-I (X) was readily obtained. The 3-iodo derivative of I was also prepared, but chlorination of I led to a variety of chemically interesting products, including the 3-chloro and 2,3-dichloro derivatives, 2,3-dichloro-2,3-dihydro-I-sulfoxide, a trichloro-2,3-dihydro-I-sulfoxide, and the sulfone. An additional scheme is presented to show further conversions of the bromo compound X to other derivatives from which the thienopyridine analogs of tryptamine and tryptophan should be quite readily obtainable. Scheme 3 shows a beginning for a route to analogous 2-substituted-I compounds; and scheme 4 depicts the practical 4 step synthesis of thieno-/3,4-c/pyridine, (the last of the 6 possible thienopyridines to be synthesized) which was achieved from the commercially available 3,4-dimethylpyridine. 4 references. (Author abstract modified)

075105 Altschule, Mark D.; Nayak, Ullhas. Department of Medicine, Harvard Medical School, Boston, Massachusetts 02115 Epinephrine-cyclizing enzyme in schizophrenic serum. Final Report, NIMH Grant MH-15697, 1970. 5 p.

A study shows that an epinephrine cyclizing catalyst is present in normal human serum. The activity of this system is not increased in patients with a diagnosis of schizophrenia. In fact some of their values appear to be low; but low values found in some chronic schizophrenic patients cannot be phsyiologically significant. The values in 11 chronic schizophrenic patients lay between 1.25 and 2.8; the 2 patients with the syndrome of recent onset had values below 1.0uu moles/ml/hour. Two of the chronic patients and one of the acute patients were not receiving drugs at the time of the study. 26 references.

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

074685 Julou, L.; Ducrot, R.; Bardone, M. C.; Garret, C. Laboratoires de Recherches de la Societe des Usines Chimiques Rhone-Poulenc, 94, Vitry-sur-Seine, France /Current conceptions on certain aspects of the pharmacology of neuroleptics./ Conceptions actuelles sur certains aspects de la pharmacologie des neuroleptiques. *Laval Medical (Quebec).* 41(6):845-857, 1970.

Nine laboratory tests were conducted on animals to explore the idea of experimental activity spectrum of neuroleptics and the individual pharmacological profile. Six phenothiazine derivatives were studied in comparison with chlorpromazine. The predictive values of the tests were proved in regard to the following effects: 1) antipsychotic effects; 2) sedative actions antagonistic to psychotic excitation; and 3) side effects. Drawbacks of these methods of research for new neuroleptics as far as human correlations are concerned are pointed out. The major hope in psychopharmacological research for new neuroleptics lies in the growth of knowledge on the mechanisms of action in this type of drug, and refers more specifically to the action of the products on the metabolism of the catecholamines in the central nervous system. 41 references.

03 MECHANISM OF ACTION - PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

072471 Bondareff, W.; Routtenberg, A.; Narotzky, R.; McLone, D. G. Department of Biostructure, Northwestern University Medical School, Chicago, Illinois 60611 Intrastriatal spreading of biogenic amines. *Experimental Neurology.* 28(2):213-229, 1970.

Biogenic amines were injected into the caudate nuclei of 47 awake, freely moving rats through cannulae implanted 1 week previously. After injections, the brains were freeze dried and treated

with formaldehyde vapors according to the method of Falck and Hillarp. Intrastriatal spreading was determined by fluorescence microscopy. Intrastriatal spread of catecholamines related directly to both concentration and osmolality of injected amine. Dopamine and norepinephrine, 1 microgram/microliter saline were found to spread rostral caudally, mean total distances of 2.11 and 1.88 mm, respectively. Intrastriatal spreading was affected by dexamethasone and mannitol, which reduced rostral caudal spreading of dopamine by more than 50 percent when administered prior to intrastriatal injection. Spreading of serotonin through brain tissue could not be determined. The spreading of exogenous catecholamines through cerebral tissues may occur through extracellular channels. The observed rate ofspreading (about 0.5mm/min) and electron microscopic analysis were consonant with this interpretation. 49 references. (author abstract modified)

072525 Langslet, Asbjorn. Institute of Aviation Medicine, Royal Norwegian Air Force, Oslo, Norway ECG-changes induced by phenothiazine drugs in the anaesthetized rat. ***Acta Pharmacologica et Toxicologica (Kobenhavn).*** **28(4):258-264, 1970.**

The ECG has been recorded in barbiturate anesthetized rats during intravenous infusion of levomepromazine, chlorpromazine, prochlorperazine and perphenazine. All the drugs decreased impulse generation and propagation in the heart. The magnitude of the changes in heart rate, PQ, QRS and QT time was dose dependent, and the relative order of potency of the drugs was as follows: perphenazine and prochlorperazine; chlorpromazine; and levomepromazine. Perphenazine, prochlorperazine, chlorpromazine and levomepromazine in 0.000025 molar concentration increased the PQ time to about 130%, 128%, 122% and 117%respectively, of the PQ time before infusion. The magnitude of the changes in rate, QT intervals and QRS intervals was in the same range. At higher concentrations, all the drugs caused AV block of variable degree. Qualitatively, these changes were similar to those induced by the drugsin the isolated perfused rat heart; quantitatively, however, these in vivo findings do not correspond to the in vitro findings. Levomepromazine which in vitro, was unique in changing the ECG pattern at much lower concentrations than the other phenothiazine derivatives, was less potent than perphenazine, prochlorpromazine and chlorpromazine in vivo. Possible explanations for this discrepancy are discussed. 11 references. (author abstract)

072579 Avakumov, V. M.; Batulin, Yu. M. Laboratoriya Psikhopharmakologii Instituta Farmakologii i Khimioterapii AMN, Moscow, U.S.S.R. /Comparative characteristics of chlorpromazine and chloracyzine distribution in rats./ Sravnitel'naya kharakteristika raspredeleniya Aminazina i khloratsizina u krys. ***Farmakologiya i Toksikologiya (Moskva).*** **33(1):14-17, 1970.**

Chloracyzine and chlorpromazine are distributed differently in the bodies of rats than other drugs administered in similar doses. Chloracyzine accumulates in the blood, myocardium and liver to a greater extent than does chlorpromazine. The content of the latter in brain tissue is higher than that of chloracyzine. 12 references. (author abstract)

072580 Lapin, I. P.; Ksenofontova, T. A.; Kvitko, I. Ya; Poray-Koshits, B. A. Leningradskiy Tekhnologicheskiy Institut im. Lensoveta, Leningrad, U.S.S.R. /Central neurotropic activity of aminopropyl and amino-propionylic derivatives of iminobenzyl and diphenylamine and its relation tolonization constants./ Tsentral'naya neyrotropnaya aktivnost'aminopropil'nykh i aminopropionil'nykh proizvodnykh iminodibenzila i difenilamina i svyaz' ee s konstantami ionizatsii. ***Farmakologiya i Toksikologiya (Moskva).*** **33(1):8-13, 1970.**

The decrease of the ionization constant (pKa) for amino-propionylic iminodibenzyl derivatives is followed by a decrease or even a complete disappearance of the typical pharmacological effects of antidepressants, viz. antireserpine, adrenopositive and anticholinergic. It is assumed that for the appearance of the indicated properties, the pKa values of aminopropionylic (and probably the others) derivatives of iminodibenzyl group should be higher than 8.3. No correlation between the toxicity of the preparations tested and the values of their pKa could be established. 15 references. (author abstract modified)

072586 Bernareggi, V.; Bugada, G.; Levi, G. Research Department of Valeas, s.a.s., Via Vallisneri, 10/12, 20133 Milan, Italy Absorption and pharmacological activities of a new diazepam preparation. ***Arzneimittel-Forschung (Aulendorf).*** **20(9):1230-1232, 1970.**

The blood levels of a new more lipid soluble pharmaceutical form of 7-chloro-1,3-dihydro-1-methyl-5mphenyl-2H-1,4-benzodiazepin-2-one (diazepam), namely Lipodiazepam are evaluated in comparison with diazepam powder and diazepam solution after oral administration in mice and rabbits. The muscle relaxant effect of the 3 forms in mice was established by the tests of swimming and of rotating bar. Lipodiazepam showed a faster absorption in comparison with diazepam powder and a more prolonged activity than diazepam powder and diazepam solution. 6 references. (author abstract)

072589 Heykants, J. J. P.; Lewi, P. J.; Janssen, P. A. J. Janssen Pharmaceutica n. v., Research Laboratories, Beerse, Belgium On the distribution and metabolism of neuroleptic drugs. Part 2: pharmacokinetics of moperone. ***Arzneimittel-Forschung (Aulendorf).*** **20(9):1238-1242, 1970.**

The distribution, metabolism and excretion in rats of 4'-fluoro-4-(4-hydroxy-4-p-tolylpiperidino) butyro-phenone hydrochloride (moperone), were studied in brain, liver, blood, urine and feces after s.c. administration of the specifically tritium labeled drug. The experimental data were analysed by IBM-1800 computer, using polynomial regressions. After 0.5hr, the relative increases in brain and liver are significantly smaller than corresponding increases of initial dose. The ratios of unmetabolized drug to total amounts of drug are dose dependent. Brain levels can reach a tenfold of the corresponding blood levels. Moperone is rapidly metabolized in the liver, as opposed to its prototype compound haloperidol. A model is developed based on saturable brain and liver compartments. Stereotyped behavior of the rat induced by amphetamine and apomorphine is antagonized by median effective doses corresponding to moperone levels in brain of 70 and 315 nanograms, respectively. 7 references. (author abstract)

073069 Simmonds, M. A.; Uretsky, N. J. School of Pharmacy, 29/39 Brunswick Square, London W. C. 1, England Central effects of 6-hydroxydopamine on the body temperature of the rat. ***British Journal of Pharmacology (London).*** **40(4):630-638, 1970.**

In view of the accumulated evidence suggesting a role for noradrenaline (NA) in the central control of body temperature in the rat, the effects of 6-hydroxydopamine (6-OHDA) on its thermoregulation were investigated. Rats which had been pretreated with intraventricular injections of 6-hydroxydopamine (6-OHDA) to cause a selective depletion of brain NA to 20.7% of control brain NA and brain dopamine (DA) to 34.6% of control brain DA retained an unimpaired ability to regulate their body temperatures on exposure to heat or cold. This is discussed in relation to the possible role of brain NA in the central control of body temperature. Intraventricular injections of 6-OHDA in normal rats at room temperature caused an acute, dose dependent hypothermia of up to 4.5degrees C which lasted for 4 to 5 hours. Depletion of brain NA and DA by prior treatment with 6-OHDA markedly reduced the hypothermic response to a subsequent dose of 6-OHDA. Selective depletion of brain NA without affecting brain DA did not reduce the response to 6-OHDA. The acute hypothermic response to 6-OHDA, may therefore, be related to a release of DA in the brain. 22 references. (Author abstract modified)

073327 Marks, Neville. New York State Institute for Neurochemistry and Drug Addiction, Ward's Island, New York, N.Y. 10035 Some neurochemical correlates of axoplasmic flow. ***Clinical and Basic Research.*** **31(11):5-13, 1970.**

The present study was designed to repeat measurements of peptide hydrolases (amino and carboxypeptidases and arylamidases) and peptidyl-peptide hydrolases, in different examples of peripheral nerve preparations in order to determine if proximodistal gradients existed in the different nerve segments. The enzymes were analyzed by previously published methods in the unmyelinated walking nerve of lobster and crab, in the myelinated sciatic nerve of the frog and rat. In view of the importance placed on the central origin of many axoplasmic components, also analyzed were the different gradients in brain region of the lobster compared to different segments of the ventral cord. The opportunity was taken, also, to measure the associated pools of ninhydrin positive material (peptides and amino acids) since these represent the end products od degradation and many reflect the turnover and movement of axoplasmic components. 25 references.

073681 Val'dman, A. V.; Lebedeva, M. N. Kafedra Farmakologii I Leningradskogo Meditsinskogo Instituta imeni I.P. Pavlova, Leningrad, U.S.S.R. /The catecholamine content in the brain

stem of albino rats in the development of tolerance to tryphtazine./ Soderzhaniye katekholaminov v stovole mozga belykh krys pri razvitii tolerantnosti k triftazinu. *Byulleten' eksperimental'noy biologii i meditsiny, Moskva.* 70(8):51-53, 1970.

The level of catecholamines in the brain stem of albino rats during chronic (daily) three month long subcutaneous injections of tryphtazine (2mg/kg) was determined. A single injection of tryphtazine causes a significant reduction of the noradrenaline level in the brain stem. In 2 weeks the noradrenaline content rapidly grows; signs of tolerance (according to behavior tests) at this period are not observed. A complete restoration of the catecholamine level takes place in 3 months and coincides with the development of tolerance according to the conditioned reflex test. 13 references. (author abstract)

073709 Eckert, H.; Hopf, A. Biochem. Laboraztorien, Pharmazeut. Department, Sandoz AG, 4000 Basel, Switzerland Autoradiographic studies on the distribution of psychoactive drugs in the rat brain: IV. C14-thioridazine. *International Pharmacopsychiatry.* 4(1-2):98-116, 1970.

The distribution of C14-thioridazine was studied in 75 regions of the rat brain, using autoradiograms of sagittal serial section 5, 30 and 60 min, 2, 4, 8 and 24 hr after intravenous injection. The contents of labelled substance in the various brain regions were determined by photometry. After longer intervals the highest values were found in the hippocampus, which showed an interesting distribution pattern. Activities were low in the hypothalamus, the reticular formation and in the nuclei of the extrapyramidal motor system with the exception of the striatum, which had average activities. The distribution pattern of C14-thioridazine was compared with the numerical and volume density of nerve and glial cells, the capillary density, the contents of oxidative enzymes, the lipid contents, the incorporation of labelled amino acids and other histochemical patterns and chemical parameters. No meaningful correlation emerged however. It can only be concluded that many factors determine the distribution of the drugs; the relative importance of these various factors, however, is still unknown. The pattern found is similar to those patterns described of other psychoactive drugs (neuroleptics, antidepressive and psychotomimetic compounds) and it is possibly a prerequisite of an action in the psychic sphere. 38 references. (author abstract)

073715 Komissarov, I. V.; Talalayenko, A. N. Kafedra farmakologii Donetskogo meditsinskogo instituta, Donetsk, U.S.S.R. /An analysis of receptive structures participating in the behavior reactions of cats induced by catecholamines and serotonin./ K analizu retseptivnykh struktur, uchastvuyushchikh izmeneniyakh povedencheskikh reaktsiy koshek, vyzvannykh katekholaminami i serotoninom. *Byulleten' eksperimental'noy biologii i meditsiny (Moskva).* 70(9):42-45, 1970.

In experiments on cats, changes in the motor and vegetative components of behavior reactions induced by intraventricular brain injection of catecholamines, serotonin and their antagonists were investigated. Noradrenaline, adrenaline, mesatone and serotonin produced a motor inhibition in animals. Isadrine was ineffective. Propranolol and morphine did not alter, whereas dehydroergotamine and phentolamine shortened the period of motor inhibition caused by noradrenaline. Morphine did not change the motor activity induced by serotonin, but was inhibited by dehydroergotamine and LSD. The results testify to the fact that motor inhibition due to bioamines was associated with the action on the alpha-adreno- or M-serotoninosensitive cerebral structures. Serotonin induced excitation occurs via D-serotonin receptors. 15 references. (author abstract)

073716 Baru, A. M.; Bozhko, G. Kh. Khar'kovskiy nauchno-issledovatel'skiy institut nevrologii i psikhiatrii, Khar'kov, U.S.S.R. /The effect of some inhibitors and metabolites of catecholamine on the processes of fixation and reproduction of 'memory traces'./ Vliyaniye Nekotorykh inhibitorov i metabolitov obmena katekholaminov na protsessy zakrepleniya i vosproizvedeniya 'sledov pamyati'. *Byulleten' eksperimental'noy biologii i meditsiny (Moskva).* 70(9):45-48, 1970.

The formation and reproduction of conditioned defense reaction of avoidance (CDRA) in albino Wistar rats were investigated after the administration of substances acting upon the catecholamine metabolism. Disulfiram inhibits the noradrenaline synthesis and sharply depresses the reproduction of steadily evolved CDRA; this effect may be prevented by preliminary introduction of monoamineoxidase (iprazid) inhibitor. In some animals with an inability to learn (due to spontaneous or induced shock with an electric current 3 to 4 times higher than the threshold), iprasid was conducive to reinforcement of CDRA. A

chronic introduction of 3,4-dimethoxyphenylethylamine impeded the formation of CDRA, whereas in single injection it inhibited the preliminary evolved reaction. The possible role of catecholamines in processes of formation and reproduction of memory traces is discussed. 14 references. (author abstract)

073717 Krylov, S. S.; Snegirev, Y. E. A. Institut toksikologii Ministerstva zdravookhraneniya SSSR, Leningrad, U.S.S.R. /The effect of aminoesters of substituted glycolic and acetic acids on the content of noradrenaline in the brain of rats./ Vliyaniye aminoefirov zameshchennoy glikolevoy i uksusnoy kislot na soderzhaniye noradrenalina v golovnom mozgu kpys. *Byulleten' eksperimental'noy biologii i meditsiny (Moskva).* 70(9):49-52, 1970.

Aminoesters of diphenylglycolic acid (amizyl and glipin in a dose of 40mg/kg, N-methyl-4-oxypiperidylbenzylate, 10mg/kg i.p.)caused in rats motor excitation, and reduction of the level of noradrenaline in the cerebral tissues. An analogous effect was observed when phenamine (5mg/kg) was given to rats. The dynamics of changes in the content of noradrenaline in the brain correlated with the altered behavior of the animals. Aminoesters of diphenylacetic acid (diphacyl and tropacin, 40mg/kg) caused an opposite effect: inhibition of the motor activity of animals and an increased noradrenaline content in the brain. Derivatives of glycolic acid are, like phenamine, capable of freeing from the labile - bound depot, noradrenaline in a physiologically active state. This causes the development of motor excitation in animals. The mechanism of increase of the noradrenaline level in the brain in the action of acetic analogs remains obscure. 28 references. (author abstract)

074084 de la Torre, J. C.; Mullan, S. Division of Neurological Surgery, The University of Chicago Hospitals, 950 East 59th Street, Chicago, Illinois 60637 A possible role for 5-hydroxytryptamine in drug-induced seizures. *Journal of Pharmacy and Pharmacology (London).* 22(11):858-859, 1970.

A possible role of 5-hydroxytryptamine (5-HT) in drug induced seizures in rats is proposed. The pattern of convulsive seizures seen in rats injected with leptazol (pentylenetetrazol) was used to test the anticonvulsive properties of several drugs that affect brain monoamine metabolism. The index used for measuring the seizures is presented. The relative seizure susceptibility to leptazol after various drugs is presented and discussed. The results of the experiments suggest that affecting brain 5-HT levels with 5-hydroxytryptophan (5-HTP) in conjunction with a peripheral decarboxylase inhibitor may result in decreased neuronal excitability induced by leptazol. It seems, also, that adequate penetration of 5-HTP into brain tissue cannot be achieved without prior inhibition of peripheral decarboxylase activity. 9 references.

074131 Vernadakis, Antonia. Department of Psychiatry, University of Colorado Medical Center, Denver, Colorado 80220 Effects of chlorpromazine on convulsive responses in developing rats. *Experimental Neurology.* 29(3);473-482, 1970.

Five litters of rats received various doses of chlorpromazine (CPZ), either at 6, 13, 20, or 29 days after birth, and responses of the neuraxis to maximal electroshock stimulation were studies during maturation. Each litter consisted of controls and rats treated with 3, 15, 30, and 60 mg CPZ/kg body wt. The durations of hind limb flexion were generally longer (and the durations of extension were shorter) in rats receiving CPZ either at 6 or 20 days. In rats receiving CPZ at 13 days, the durations of flexion were shorter (and the durations of extension were longer) than those observed in appropriate controls. No changes were observed in 29 day old CPZ treated rats. It was concluded that CPZ administered to developing rats has both stimulant and depressant effects as assesed by responses to electroshock stimulation. Furthermore, these differential effects of CPZ appear to be age dependent, according to the maturity of the central nervous system. 19 references. (Author abstract modified)

074133 Stamenovic, B. A.; Varagic, V. M. Neurophysiological Laboratory, Institute for Medical and Technical Protection, Belgrade 7, Yugoslavia The effect of eserine on the efferent neuronal activity in the cervical sympathetic of the rat. *Neuropharmacology (London).* 9(6):561-566, 1970.

In order to evaluate the central origin of the hypertensive response to eserine, the neuronal efferent activity in the cervical sympathetic of the rat was investigated. It was found that eserine produced a significant and dose dependent increase in the neuronal activity in the preganglionicfibers of the cervical sympathetic nerve. Duration of the increased neuronal activity corresponded well to the duration of the hyperten-

sive response to eserine. Atropine completely blocked the increased preganglionic neuronal activity produced by eserine. Methyl-atropine, phentolamine, hexamethonium and reserpine pretreatment did not affect the eserine effect. It is concluded that adrenergic activation by eserine is probably preceded by the activation of cholinergic mechanisms in the brain, leading to an increased efferent activity in the cervical sympathetic system. 14 references. (Author abstract)

074818 Persson, Torgny; Waldeck, Bertil. Psychiatric Research Centre, St. Jorgen Hospital, Goteborg, Sweden A source of error in catecholamine turnover studies with labelled DOPA: slow disappearance of the precursor. ***Acta Pharmarmacologica et Toxicologica (Kobenhavn).*** **28:466-476, 1970.**

To elucidate the precursor - product relationship, a source of error on catecholamine turnover studies with labelled dopa -- the slow disappearance of the precursor, is investigated. Rats were injected with 5 micrograms/kg L-dopa, (labelled in ring-2,5,6 with 3H). At various time intervals, the animals were killed and the levels of 3H-dopa, 3H-3-methoxytyrosine (MTyr), 3H-noradrenaline (NA) and 3H-dopamine (DA) in different tissues were determined after separation on alumina and Dowex columns. The specificity of the radioactivity in the dopa and MTyr fractions was checked by radiopaper chromatography. 3H-dopa appeared to decrease almost uniformly in the different tissues examined. The concentration of 3H-dopa in the brain was low relative to the plasma and other tissues. The levels of 3H-dopa and 3H-NA in the brain were of the same order of magnitude and the compounds disappeared at about the same rate from the tissue. In the heart 3H-DA disappeared more slowly than 3H-dopa. The femoral muscle showed the largest accumulation of 3H-dopa. There was no correlation between the extent of 3H-dopa accumulation and the density of the adrenergic innervation. The data show that after injection of 3H-dopa, this compound and the intermediate product 3H-DA are present for several hours in amounts sufficient to invalidate estimations of the true turnover of NA. 3H-MTyr was eliminated very slowly from the organism. 20 references. (Author abstract modified)

074854 Sato, Hiroshi; Ohga, Akira; Nakazato, Yoshikazu. Department of Pharmacology, Faculty of Veterinary Medicine, Hokkaido University, Sapporo, Japan The excitatory and inhibitory innervation of the stomachs of the domestic fowl. ***Japanese Journal of Pharmacology (Tokyo).*** **20(3):382-397, 1970.**

The responses of the stomach to stimulation of the vagus and sympathetic nerves (perivascular nerve) were investigated in the domestic fowl anesthetized with chloralose. The responses of the proventriculus to each nerve stimulation were especially studied using cholinergic, adrenergic and ganglionic blocking agents. Stimulation of the vagus and perivascular nerves caused an excitatory and an inhibitory response of the proventriculus and gizzard respectively depending on the stimulus strength. The crop usually responded with only a contraction to vagal stimulation, but not to perivascular nerve stimulation. Most of the excitatory responses of each stomach caused by either vagal or perivascular nerve stimulation were potentiated by physostigmine and abolished by atropine. The effects of bretylium, guanethidine, adrenaline, noradrenaline, phenoxybenzamine, dibenamine, pronethalol, hexamethonium on the atropinized fowl, or in combination with other drugs, were tested, also, and the results reported. It is suggested that the vagal pathways to the crop, proventriculus and gizzard of the domestic fowl may contain cholinergic excitatory and nonadrenergic inhibitory fibers. On the other hand, the perivascular sympathetic pathway, the excitatory fibers may be both cholinergic and adrenergic, and the inhibitory one seems likely to be adrenergic. 23 references. (Author abstract modified)

074855 Chatterjee, A. K.; Ghose, A. Jiwaji Research Laboratory, Detachment, Defence Research Laboratory (Materials), Gwalior-2, India The role of methylamphetamine on plasma hexosamine level under stress. ***Japanese Journal of Pharmacology (Tokyo).*** **20(3):439-441, 1970.**

The effect of one type of body stress, work under simulated low atmospheric pressure (LAP), on plasma hexosamine level (PHL) is studied both with and without administration of the antifatigue drug, methylamphetamine, to rats. Methylamphetamine was administered intraperitoneally one-half hour before placing the animals in the low pressure chamber. It was noted that PHL is lowered under LAP (no drug). This change in PHL is in the opposite direction from that resulting from body stress in earlier experi-

ments. Lap and body stress (work on a treadmill) caused no significant decrease in PHL, but with administration of 1, 2, 3, and 5mg/kg body weight of methylamphetamine, under LAP and stress, the PHL is significantly decreased; however, there is a reversal effect with increase in dosage. It is proposed that glycoprotein is utilized under low pressure to feed an increased glycolytic process. Also, as a parallel similarity exists on the lowering of PHL and blood lacticacid under the situation, it is suggested that the lowering of hexosamine level after work in low pressure under the influence of methylamphetamine may be regarded as an indicator of the beneficial effect of the drug on exercise in low pressure. 14 references.

074861 Maitre, L.; Staehelin, M.; Bein, H. J. Biological Laboratories of the Pharmaceutical Department of CIBA Limited, Basle, Switzerland Effects of benzoctamine (30803-Ba, Tacitin), a new psychoactive drug, on catecholamine metabolism. *Biochemical Pharmacology (Oxford).* 19(11):2875-2892, 1970.

Benzoctamine (Tacitin), 1-methylamino-methyldibenzo/b,e/ bicyclo /2.2.2/ octadiene, is a new psychoactive agent which possesses tranquilizing properties. Its effects on catecholamine metabolism have been studied. Benzoctamine produced no marked change in the catecholamine concentration of various rat organs after either single or repeated treatment and did not inhibit monoamine oxidase or catechol-0-methyltransferase activities in liver and brain. It enhanced markedly the incorporation of 3H-tyrosine into 3H-catecholamines in brain and adrenals. It accelerated, also, the disappearance rate of intracisternally administered 3H-noradrenaline. 3H-Noradrenaline uptake in the rat heart and brain was not inhibited. It is concluded that benzoctamine most probably increases the turnover rate of catecholamines. 32 references. (Author abstract)

074862 Despopoulos, Agamemnon. Department of Physiology, School of Medicine, University of New Mexico, Albuquerque, New Mexico Antihemolytic actions of tricyclic tranquilizers: structural correlations. *Biochemical Pharmacology (Oxford).* 19(11):2907-2914, 1970.

The antihemolytic actions of tricyclic tranquilizers are studied to permit correlation of molecular structures with biological activities. Thirty one phenothiazines were examined for their capacity to protect red blood cells of the dog against hypoosmotic hemolysis. Incubation of erythrocytes in buffered saline (135mOsmoles/1.)resulted in 40 to 50% hemolysis. Addition of phenothiazines to this system generally reduced hemolysis. The 50% effective dose (ed50) was determined for each compound. The ed50 ranged from 0.002 to 0.043 mM. Protection against hemolysis was related to molecular structural features: substitutions at position 10 showed no predictable influence on hemolysis; 2 sulfoxides had no protective influence; protection increased with increasing electronegativity at position 2 -- CF3 greater than C1 greater than H. Imipramine and demethylimipramine also had antihemolytic activity, but the response was maximal at the smallest dose used and did not change with larger doses. In several experiments, phenothiazines were preincubated with compounds which might be constituents of the red cell membrane. Binding could not be observed between phenothiazines and lecithin or cholesterol. Extensive binding to bovine ala enivob oo bovine albumin was demonstrated. 17 references. (Author abstract modified)

074866 Lemberger, L.; Sernatinger, E.; Kuntzman, R. Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, Maryland 20014 Effect of desmethylimipramine, iprindole and DL-erythro-alpha-(3,4 dichlorophenyl)-beta-(t-butyl amino) propanol HC1 on the metabolism of amphetamine. *Biochemical Pharmacology (Oxford).* 19(12):3021-3028, 1970.

The effect of desmethylimipramine, iprindole and DL-erythro-alpha-(3,4 dichlorophenyl)-beta-(t-butyl amino) propanol hydrochloride (B.W.65-54) on the metabolism of amphetamine in the rat, rat heart and rat brain was determined. In addition the effect of B.W. 65-54 on brain levels of amphetamine in the guinea pig and rabbit was investigated. The ability of a compound to block norepinephrine accumulation or potentiate amphetamine action has been used in the past to evaluate antidepressant activity. The results presented here indicate the limitations of this approach. B.W. 65-54, desmethylimipramine and iprindole, 3 compounds having antidepressant activity, all potentiate the locomotor activity of amphetamine in rats but this effect is due to inhibition of amphetamine metabolism. Iprindole, a potent antidepressant in man, and B.W. 65-54 do not affect the levels of 3H-norepinephrine in the rat heart while, desmethylimipramine does. 24 references. (Author abstract modified)

074934 Satoh M.; Yamatsu, K.; Takagi, H. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyoto University, Shimoadachi-cho, Sakyo-ku, Kyoto, Japan Sites of action of RAM-302 and nalorphine as morphine antagonists. *Neuropharmacology (London).* 9(6):533-538, 1970.

Sites of antagonistic and agonistic actions of RAM-302 (N-propargyl-14-hydroxy-dihydronormorphinone hydrochloride) and nalorphine were investigated using evoked potentials in cat. The suppressive effects of morphine on evoked potentials recorded from the cerebral cortex, reticular formation and the ventrolateral tract of spinal cord following electrical stimulation of the splanchnic or sciatic nerve and the augmenting response were antagonized by RAM-302 or nalorphine. The potency of the morphine antagonistic action of RAM-302 was nearly equal to that of nalorphine in all responses tested. The inhibitory actions of RAM-302 and nalorphine per se on afferent pathways of the splanchnic nerve were observed in unanesthetized cat at dose levels comparable to the suppressive doses of morphine but not in anesthetized cat, even with larger doses. These drugs had no inhibitory effects on the augmenting response in the unanesthetized state. 18 references. (Author abstract)

074936 Herz, A.; Albus, K.; Metys, J.; Schubert, P.; Teschemacher, H. Max-Planck-Institut fur Psychiatrie, Munchen, Germany On the central sites for the antinociceptive action of morphine and fentanyl. *Neuropharmacology (London).* 9(6):539-551, 1970.

The inhibition by morphine and fentanyl of a nociceptive response, the licking reaction elicited by electrical stimulation of the tooth pulp, was studied in rabbits. Both drugs were injected into the entire ventricular system, and into its separate parts and morphine was applied to definite brain structures. Spread of the applied drug was examined autoradiographically, using 14C labelled morphine. Intraventricular injection of morphine was 500-1000 times more effective than intravenous injection. The onset of action was much slower than after systemic application; this latency is interpreted as being caused by the slow permeation of morphine to the receptor areas in the periventricular structures. Injection into separate parts of the ventricular system did not inhibit the nociceptive reaction when the spread of substance was restricted to 1 or both lateral ventricles. Inclusion of the third ventricle in the area of distribution resulted in only a slight increase in effectiveness. Application of the drugs into the aqueduct and into the fourth ventricle induced a complete inhibition of the nociceptive reaction. When morphine spread into the surrounding of the cisterna cerebellomedullaris (with exclusion of ventricular system) no effect was observed. Uni- or bilateral microinjection of morphine into various diencephalic and mesencephalic periventricular structures induced a pronounced inhibition of the nociceptive reaction. The most effective sites of the antinociceptive action of morphinelike substances were situated in the fossa rhomboides and structures near it. The functional structures involved in the drug effects are discussed. 40 references. (Author abstract modified)

074939 Borbely, A. A.; Hall, R. D. Department of Pharmacology, University of Zurich, Zurich, Switzerland Effects of pentobarbitone and chlorpromazine on acoustically evoked potentials in the rat. *Neuropharmacology (London).* 9(6):575-586, 1970.

The effects of pentobarbitone and chlorpromazine on click evoked potentials from the rat's auditory cortex, medial geniculate body, and hippocampus were investigated. Amplitude and latency measures made on sliding averages by a computer provided essentially continuous measurement of evoked responses throughout long experiments. Following a large dose of pentobarbitone (60mg/kg) amplitudes of the several components of cortical responses displayed characteristic patterns of change that were readily apparent in the computer displays. Early deflections, for example, showed an initial rapid increase in amplitude, followed by a more gradual increase during deep anesthesia; they became suddenly very large at an early recovery stage and finally diminished slowly in a later recovery period. Late waves followed their own courses, were much reduced during deep anesthesia, and were generally large during late recovery periods when, however, they displayed large fluctuations in amplitude. In contrast, peak latencies of all components were increased in a relatively simple way. Early waves in medial geniculate body responses behaved like early cortical deflections, while late waves looked and behaved like hippocampal responses, disappearing during deep anesthesia. Chlorpromazine increased the amplitudes and latencies of all cortical deflections, while early medial geniculate body components

showed similar, though smaller, changes. Waveforms of hippocampal responses were significantly modified by chlorpromazine, and peak latencies were increased, as they were at all sites. 25 references. (Author abstract)

075275 Stone, Eric A. The Rockefeller University, New York, N. Y. 10021 Swim-stress-induced inactivity: relation to body temperature and brain norepinephrine, and effects of d-amphetamine. *Psychosomatic Medicine*. 32(1):51-59, 1970.

Rats given a 20 min swim stress at 14.5C show a precipitous drop in body temperature to 21-22 C, and a profound depression in exploratory activity lasting 2 hr. This is associated with a reduction of brain norepinephrine, an absence of decline in specific activity over this period, and an increased retention of H3-norepinephrine, suggesting that the synthesis and possibly the release of brain norepinephrine is inhibited by the stress. d-Ampetamine, 4mg/kg, given immediately after the stress causes a restoration of exploratory activity without elevating body temperature. It also prevents the reduction of brain norepinephrine and lowers the elevated specific activity, but has little effect on the increased retention of H3-norepinephrine. Possible mechanisms of this action and its relation to behavior are discussed. 32 references. (Author abstract)

075276 Levine, Robert J.; Senay, Edward C. Departments of Internal Medicine and Pharmacology, Yale University School of Medicine, New Haven, Connecticut 06510 Studies on the role of acid in the pathogenesis of experimental stress ulcers. *Psychosomatic Medicine*. 32(1):61-65, 1970.

Previous studies have provided strong evidence to support the concepts that in the rat histamine is the chemical mediator of gastric acid secretion and that histamine plays an essential role in the pathogenesis of stress ulcers. The present experiments indicate that the role of histamine in the pathogenesis of stress ulcers in rats is probably mediated through stimulation of gastric acid secretion. In particular, a strong negative correlation was found between intragastric pH and the incidence of stress ulcers. Furthermore, intragastric administration of Basal jel (a nonabsorbable antacid) afforded significant protection against stress ulcers without preventing the sharp increase in histidine decarboxylase activity in response to stress. 10 references. (Author abstract)

075438 Boles, John; Russell, Roger W. Department of Psychology, Indiana University, Bloomington, Indiana Relations between the electrogastrogram and gastric ulceration during exposure to stress. *Psychophysiology*. 6(4):404-410, 1970.

Relations between development of gastric ulceration and changes in motility of the stomach, as recorded by the electrogastrogram (EGG), were studied under conditions where subjects (Ss) rats, were exposed to physical (immobilization) and chemical (reserpine) stressors and to the two in combination. Following 36 hrs of the various treatment, all restraint plus reserpine (Ss) were ulcerated; 60% of the restraint only (Ss) had lesions; and, only three of ten no restraint (Ss) showed gastric damage. The same rank order was obtained for the mean number of lesions per group. There were no significant differences among groups in total acidity of the stomach at autopsy immediately after their experimental treatments. The restraint only groups showed a trend toward increased gastric motility during the treatment period, while the restraint plus reserpine groups showed a progressive decrease in motility, the divergence leading to statistically significant differences as exposure to the different stressors continued. The results do not support the hypothesis that the experimentally produced lesions are related to an increase in gastric acidity; they do support the hypothesis that the experimentally produced lesions are related to an increase in gastric acidity; they do support the hypothesis that the ulceration is related to changes in gastric motility, more severe lesions appearing in (Ss) whose motility decreased during the treatment period. 13 references. (Author abstract)

075665 Brown, Gregory M.; Grota, Lee J.; Penney, David P.; Reichlin, Seymour. Clarke Institute of Psychiatry, 250 College Street, Toronto 180, Ontario, Canada Pituitary-adrenal function in the squirrel monkey. *Endocrinology*. 86(3):519-529, 1970.

During the course of neuroendocrine investigations in squirrel monkeys (Saimiri sciureus), 'base line' values for plasma corticoids by radiostereoassay in excess of 400 micrograms/100ml were observed. These values are higher than any reported in other mammalian species. Among possible explanations of this finding is that these animals are resistant to feedback inhibition of adrenocorticotropin (ACTH) release, that there is an unusual circulating corticoid dif-

ferent from cortisol, or that there is an unusually high concentration of cortisol binding protein in this species. In order to answer these questions, studies have been made of the nature of the corticoids and the capacity of corticoid binding proteins of squirrel monkey plasma, the rate of dissappearance from the circulation of injected 3H-cortisol, and the effects of capture, chair restraint, dexamethasone and ACTH on plasma cortisol. These studies indicate that the major steroid in squirrel monkey plasma is cortisol, that the values in resting, undisturbed caged animals are indeed uniquely high (405 micrograms/100ml + or - standard error 43) and are capable of increasing in response to capture and chair restraint, that the turnover rate of cortisol is extremely high, that adrenal function in these animals is inhibited only by relatively large doses of dexamethasone, and that they are relatively unresponsive to exogenous ACTH. 33 references. (Author abstract modified)

075714 Mueller, Robert A.; Thoenen, Hans; Axelrod, Julius. Department of Anesthesia, Northwestern University Medical School, 303 East Chicago Avenue, Chicago, Illinois 60611 Effect of pituitary and ACTH on the maintenance of basal tyrosine hydroxylase activity in the rat adrenal gland. ***Endocrinology.*** **86(4):751-755, 1970.**

The effect of pituitary and adrenocorticotropin (ACTH) on the maintenance of basal tyrosine hydroxylase activity in the rat adrenal gland is investigated in studies on normal, sham hypophysectomized and hypophysectomized male rats. Adrenal tyrosine hydroxylase in the rats has a half life (t1/2) of about 10 days after hypophysectomy. Adrenal denervation leads to a decline of this enzyme at a t1/2 of about 21 days ACTH, but neither high doses of glucocorticoids nor thyroxine prevents the decrease in adrenal tyrosine hydroxylase resulting from hypophysectomy and denervation. High doses of ACTH do not produce an increase in adrenal tyrosine hydroxylase in normal rats. Low doses of metyrapone do not interfere with the increase in tyrosine hydroxylase by ACTH in hypophydectomized animals but large doses of this drug elevate adrenal tyrosine hydroxylase. The rise caused by metyrapone can be abolished by adrenal denervation. It is concluded that the normal maintenance of adrenal tyrosine hydroxylase requires ACTH. 10 references. (Author abstract modified)

075715 Thoenen, Hans; Mueller, Robert A.; Axelrod, Julius. Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, Maryland 20014 Phase difference in the induction of tyrosine hydroxylase in cell body and nerve terminals of sympathetic neurones. ***Proceedings of the National Academy of Sciences.*** **65(1):58-62, 1970.**

The phase difference in the induction of tyrosine hydroxylase in cell body and nerve terminals of sympathetic neurones has been demonstrated in studies on male rats. The induction of tyrosine hydroxylase in the nerve terminals of the rat heart of reserpine lags behind that in the stellate ganglion by 2 to 3 days. Cycloheximide given 3 days after reserpine blocks the further rise of the enzyme in the nerve terminals. The increase in tyrosine hydroxylase activity of the lumbar ganglion is as marked as that in the stellate ganglion. The increase of enzyme activity in the sciatic nerve after reserpine administration resembles that found in the heart nerve terminals. Determination of enzyme activity in segments of sciatic nerves indicates a 2 day lag and then a proximal distal transport of enzyme, but the apparent rate is not sufficient to account for the increase in enzyme in the nerve terminals. These findings are compatible with the local synthesis of induced tyrosine dydroxylase in the nerve terminals rather than the peripheral movement of the completed enzyme. 13 references. (Author abstract modified)

075842 Friedman, Matthew J.; Wikler, Abraham. Department of Psychiatry, University of Kentucky College of Medicine, University of Kentucky Medical Center, Lexington, Kentucky 40506 The effect of intrahypothalamic microinjection of hemicholinium (HC-3) on the hippocampal theta rhythm of cats. ***Psychopharmacologia (Berlin).*** **17:345-353, 1970.**

In order to better understand the relationship between hippocampal theta rhythm and impairment of learning, both effects within the capacity of belladonna alkaloids suggesting that a relationship exists, experiments on the effects of hemicholinium (HC-3) were made. Acute and chronic intact cat preparations were made with recording electrodes located in the dorsal hippocampus and cerebral cortex, stimulating electrodes in the mesencephalic reticular formation, and an 'injectrode' in the posterior hypothalamus through which both electrical and pharmacological stimulation could be applied. In all preparations 12 to 200micro g HC-3, administered through the

'injectrode', suppressed the hippocampal theta rhythm previously elicited by electrical stimulations of either the reticular formation or the posterior hypothalamus. The latency for this effect ranged from 90 min to 3 hours. Reticular induced desynchronization of the cortical electroencephalogram (EEG) disappeared 2 to 5 hours after HC-3 administration. Reversal of the HC-3 effect on the hippocampal theta rhythm was seen shortly after administration of carbachol, bethanechol and pilocarpine. No consistent behavioral effects accompanied these changes in EEG. These findings are discussed in light of the hypothesis that HC-3 exerts a postsynaptic action in the central nervous system, although a presynaptic effect through diffusion of the injected HC-3 to a distant site cannot be ruled out with certainty. 15 references. (Author abstract modified)

04 MECHANISM OF ACTION - BEHAVIORAL

072463 Zitrin, Arthur; Beach, Frank A.; Barchas, Jack D.; Dement, William C. Department of Psychiatry, New York University School of Medicine, New York, New York 10016 Sexual behavior of male cats after administration of parachlorophenylalanine. ***Science.*** **170(3960):868-870, 1970.**

The effects of 6 or 8 daily s.c. injections of parachlorophenylalanine (150mg/kg) on the copulatory behavior in 12 male cats was studied with the use of quantitative measures of behavior shown in standard test situations with receptive females. Following injection, 6 cats showed essentially no change in intromission frequencies and 2 animals exhibited some decrease after treatment. In 90 minute tests, 7 of 8 males achieved fewer intromissions after treatment. Other measures of sexual activity, such as time before first grip, mount, or intromission, were not significantly altered by parachlorophenylalanine in any of the 12 cats. There was no noticeable difference in general behavior in the test situation, and reactions to the females, in terms of approaches or attempts to mount, failed to indicate any heightened sexual interest as a result of treatment. Seven of the 12 cats appeared less active after 5 to 7 injections. The vocalizations of these animals were softer and occurred less frequently. Brain serotonin levels were reduced in the 6 cats used for such determinations. 18 references.

072516 MacPherson, Catherine F. C.; Shek, Raymond P. N. Department of Psychiatry, Allan Memorial Institute of Psychiatry, McGill University, Montreal 110, Quebec, Canada Effect of brain iso-antibodies on learning and memory in the rat. ***Experimental Neurology.*** **29(1):1-15, 1970.**

Naive Wistar rats that had been immunized with a crude microsomal fraction from rat brain or rat liver required a greater number of trials to learn a visual discrimination problem than rats injected with saline solution. The degree of impairment of learning varied from experiment to experiment. However, analysis of variance on the results of 4 experiments showed that differences between the performances of the immunized animals and the control animals were statistically significant. When trained rats that had required a similar number of trials to learn a visual discrimination task were studied, the animals that subsequently were immunized for 1 month with rat brain or rat liver proteins performed the learned task and learned a new problem as well as the control animals that had been injected with saline solution. However, when reversal of the discrimination problem was studied, the immunized animals required fewer trials to learn the reversal than the controls. Animals immunized with hen egg albumin behaved like animals injected with saline solution. The results suggest that species specific antigens play as important a role as brain specific antigens in the brain cells responsible for memory and learning. 37 references. (author abstract)

072524 Albanus, Lennart. Pharmacology Section, Division of Experimental Defense Medicine, Research Institute of National Defense, Department 1, Stockholm, Sweden Central and peripheral effects of anticholinergic compounds. ***Acta Pharmacologica et Toxicologica (Kobenhavn).*** **28(4):305-326, 1970.**

The pharmacological effects of aryl and cycloalkylaryl glycolates of piperidine, tropine and quinuclidin have been studied in relation to atropine and scopolamine. Peripheral effects (heart rate, salivation, pupil size) have been studied in dogs in relation to their behavioral effects under standardized conditions. The anticholinergic activity was further investigated on the mouse pupil and on the blood pressure response to acetylcholine in cats anesthetized with pentobarbital. In dogs, all the glycolates elicited behavioral effects, especially on locomotion, similar to those

seen following atropine and scopolamine. Even high doses of methyl atropine produced effects indistinguishable from those produced by atropine and scopolamine. The most active compounds affected behavior at a dose of 10 micrograms per kilogram body weight given subcutaneously. All compounds elicited anticholinergic activity such as tachycardia, mydriasis, inhibition of salivation and block of acetylcholine hydrochloride response. The most potent compounds on behavior were quinuclidinylesters of phenyl and or thienyl glycolic acid which also had the strongest and most prolonged classical anticholinergic effects. The results indicate that behavioral effects are related to anticholinergic activity but that other factors such as lipid solubility and metabolism interfere with the central activity. 13 references. (author abstract)

072531 Carlini, Elisaldo A.; Masur, Jandira. Departmento de Ciencias Fisiologicas, Faculdade de Ciencias Medicas de Santa Casa, Rua Cesario Motta Jr., 112, Sao Paulo, Brazil Development of fighting behavior in starved rats by chronic administration of (-)delta-9-trans-tetrahydrocannabinol and cannabis extracts: Lack of action of other psychotropic drugs. *Communications in Behavioral Biology.* 5(1):57-61, 1970.

Starved rats injected daily with 10mg/kg of cannabis extracts or 2.5, 5.0, and 10mg/kg of (-)delta-9-trans-tetrahydrocannabinol showed striking fighting behavior after 3 to 14 days of treatment. However, such aggressive behavior was not elicited in similarly starved subjects of the same age, sex, and strain by injections of caffeine (50, 100, and 200mg/kg), amylobarbitone sodium (20mg/kg), or d,l-amphetamine sulfate (2 and 4mg/kg). Furthermore, mescaline sulfate (40mg/kg), LSD-25 (0.2mg/kg), and d,l-amphetamine sulfate (1.0and 5.0mg/kg) also failed to induce fighting behavior in starved rats previously rendered aggressive by chronic pretreatment with cannabis extract. 21 references. (author abstract)

074053 Evetts, K. D.; Uretsky, N. J.; Iversen, L. L.; Iversen, S. D. Department of Experimental Psychology, University of Cambridge, Cambridge, England Effects of 6-Hydroxydopamine on CNS Catecholamines, spontaneous motor activity and amphetamine induced hyperactivity in rats. *Nature (London).* 225(5236):961-962, 1970.

A study of the effects of 6-hydroxydopamine (6-0HDA) on rats, in whom hyperactivity had been induced with amphetamine, is reported. A baseline of activity had previously been established for the rats using photocell activity boxes. Suitable experimentals assured the exclusion of extraneous stimuli. Anesthetized rats were then administered 6-OHDA directly into the brain. Two larger doses of 6-OHDA, 250 mircograms each, caused a significant reduction in activity. Results show that amphetamine stimulates motor activity in the rat even after the substantial depletion of brain catecholamines induced by 6-0HDA. Although brain catecholamines have been implicated in a wide variety of important behavioral and physiological functions, gross depletion of the amines by 6-OHDA do not seem to produce correspondingly large changes in behavior. 11 references.

074086 Langwinski, R. Department of Pharmacodynamics, School of Medicine, Lublin, Staszica 4, Poland Stereotyped behaviour induced by (-)-ephedrine in rats. *Journal of Pharmacy and Pharmacology (London).* 22(11):874, 1970.

There appear to be no published reports implicating (-)-ephedrine in stereotyped behavior, even though it is a beta-hydrozylated derivation of methamphetamine. The induction of stereotyped behavior in rats by (-)-ephedrine is now reported. Rats were injected intraperitoneally with 40 to 140mg/kg of (-)-ephedrine. Up to 80mg/kg, the drug induced only sniffing and noncontinuous licking and biting. Higher doses, to 140mg/kg, caused sniffing at the floor and continuous licking and biting, the stereotypy resembling that produced by amphetamine. Observations were made on other drugs in conjunction with (-)-ephedrine and amphetamine. 8 references.

074145 Stromberg, U.; Svensson, T. H.; Waldeck, B. Department of Pharmacology, University of Goteborg, Goteborg, Sweden On the mode of action of amantadine. *Journal of Pharmacy and Pharmacology (London).* 22(12):959-962, 1970.

Research on the mode of action of amantadine is reported in a letter to the editor. Some functional and biochemical aspects of the effect of amantadine in central and peripheral catecholamine neurons are examined; and the mode of action of amantadine is compared with (+)-amphetamine in studies on mice. Amantadine hydrochloride (HC1) injected (150mg/kg) mice

pretreated with reserpine (10mg/kg) were tested for motility. Pre- and posttreatment with alpha-methyltyrosine methylester and L-dopa, respectively, was given to some mice, also. For assay, some mice were injected with amantadine HC1 or (+)-amphetamine sulfate, with reserpine and nialamide pretreatment. Statistical evaluation showed that amantadine caused an increased motor activity in the reserpine pretreated mice which was inhibited by alpha-methyltyrosine. A small dose of L-dopa, causing no motor stimulation by itself, restored the amantadine effect. The results indicate that amantadine requires small amounts of catecholamines for its motor stimulant effect. The results of analyses showing the effect of amantadine and (+)-amphetamine on L-dopa induced accumulation of noradrenaline, dopamine and methoxytyramine of heart and brain tissues are presented and discussed. The activity of amantadine against parkinsonism is considered. 17 references.

074147 Ho, Beng T.; Huang Jen-Tzaw. Texas Research Institute of Mental Sciences, Houston, Texas 77025 Effects of mescaline and 2,5-dimethoxy-4-methylphenethylamine on sleeping time in mice. ***Journal of Pharmacy and Pharmacology (London).*** **22(12):949-951, 1970.**

The effects of mescaline and 2,5-dimethoxy-4-methylphenethylamine (DMM-PEA) on sleeping time in mice are investigated and the results reported in this letter to the editor. Mice were injected with 50 micromol/kg of mescaline or 40mg/kg of sodium pentabarbitone and 100 microcuries of 14C labelled pentobarbitone in saline were administered. The distribution of radioactivity in mouse plasma, brain, liver and kidney was determined, as was the effect of DMM-PEA and mescaline on the barbitone and pentobarbitone sleeping time in mice. It was found that mescaline had no effect on the metabolism of pentobarbitone or on the barbitone sleeping time in mice; however, mescaline caused increases in accumulation of pentobarbitone in the mouse tissues but shortened the pentobarbitone sleeping time. The results are discussed in relation to free and bound pentobarbitone. 5 references.

074149 Leonard, B. E.; Wiseman, Barbara D. Pharmacology Section, ICI Ltd., Pharmaceuticals Division, Alderley Park, Macclesfield, Cheshire, England The effect of ethanol and amphetamine mixtures on the activity of rats in a Y-maze. ***Journal of Pharmacy and Pharmacology (London).*** **22(12):967, 1970.**

An investigation was made to determine whether ethanol shares with barbiturates the ability potentiate the effect of amphetamine on the performance of rats in a Y-maze. The results are reported in a letter to the editor. Ethanol and (+)-amphetamine were administered intraperitoneally to rats in doses of 50-800mg/kg and 4mg/kg or amphetamine. It was found that higher doses of ethanol decreased the exploratory activity, and amphetamine, even at the lower dose, increased the Y-maze activity. Combined administration of the drugs made it apparent that the depressant effect of ethanol was antagonized by amphetamine but at no dose combination did the activity of the rats approach that produced by amphetamine alone. The mechanism of action is discussed. 3 references.

074422 Miller, Roy C.; Miller, Edward K. Department of Mathematics, Gunston School, Arlington, Virginia 22206 Lack of a long-term effect of LSD on Y-maze learning in mice. ***Nature (London).*** **228(5276):1107-1108, 1970.**

Because of controversy regarding potential long-term psychological effects of lysergic acid diethylamide-25 (LSD), an examination was undertaken to determine the effect on learning of shock avoidance by repeated treatment of mice with increasing quantities of LSD over a long period. The report gives the effect of this regimen on Y-maze learning in mice; the data being consistent with a previous report of acute impariment of learning in mice as a result of LSD. But the ability of the LSD-treated mice to learn an avoidance task had returned to the level of the control mice by 3 weeks after the chronic administration of LSD. The conclusion was that there is no evidence of significant long-term impairment of learning attributable to LSD. 4 references.

074830 Clark, Carol V. H.; Gorman, Darrell; Vernadakis, Antonia. Veterans Administration Hospital, Denver, Colorado Effects of prenatal administration of psychotropic drugs on behavior of developing rats. ***Developmental Psychobiology.*** **3(4):225-235, 1970.**

The effects of prenatal administration of 1mg/kg d-amphetamine sulfate or 3mg/kg chlorpromazine HC1 to rats from days 12 through 15 of gestation inclusive were studied on behavior of

the offspring in the open field, mazes, and operant conditioning. The locomotor activity scores of rats whose mothers received chlorpromazine were significantly lower than those of controls on day 13 after birth but reached a level significantly higher than that of controls on day 18. Offspring of amphetamine treated mothers had relatively low activity scores early in testing and were delayed in reaching adult activity levels. Although in the mother - goal - maze offspring of both chlorpromazine and amphetamine treated mothers generally had shorter latencies than controls, rats whose mothers received chlorpromazine made significantly more errors. These animals also took significantly longer to acquire the bar-press response. No differences among groups were observed in learning or reversal in the T-maze or in performance or extinction of the operant response. 17 references. (Author abstract)

074865 Roth, Robert H.; Suhr, Youngmin. Department of Pharmacology, Yale University School of Medicine, New Haven, Connecticut 06510 Mechanism of the gamma-hydroxybutyrate-induced increase in brain dopamine and its relationship to 'sleep'. ***Biochemical Pharmacology (Oxford).*** **19(12):3001-3012, 1970.**

The mechanism of the gamma-hydroxybutyrate (GHB) induced increased in brain dopamine is investigated, and an attempt is made to determine if the action of GHB on dopamine containing neurons is at all related to the 'sleep' inducing properties of this agent. The naturally occurring central nervous system depressant GHB and its lactone precursor, gamma-butyrolactone (GBL) cause a marked and selective increase in brain dopamine. Concomitant with the increase in brain dopamine,homovanillic acid, a metabolite of brain dopamine, is decreased. GBL also causes a selective increase in the specific activity of brain dopamine but not of brain norepinephrine when rats are injected with C-tyrosine. This is probably the result of a compensatory activation of dopaminergic neurons because of a blockade in dopamine release induced by GHB. When catecholamine biosynthesis is inhibited by administration of alpha-methyl-p-tyrosine, GBL completely blocks the disappearance of subcortical dopamine but exerts no antagonism on the disappearance of subcortical norepinephrine. These observations are suggestive that GBL increases brain dopamine primarily by selectively blocking the release of this monoamine from dopamine containing neurons. Indirect evidence is also presented which suggests that the central nervous system depressant properties of GHB may be related to this block in the release of brain dopamine. 24 references. (Author abstract modified)

074935 Olds, M. E. Division of Biology, California Institute of Technology, Pasadena, California 91109 Comparative effects of amphetamine, scopolamine, chlordiazepoxide, and diphenylhydantoin on operant and extinction behavior with brain stimulation and food reward. ***Neuropharmacology (London).*** **9(6):519-532, 1970.**

The effects of amphetamine, scopolamine, chlordiazepoxide and diphenylhydantoin have been investigated on operant behavior for brain and food rewards. The aim was to obtain evidence for a possible mode of action of these facilitatory compounds on self-stimulation behavior. The first 3 drugs increased responding for brain reinforcement but diphenylhydantoin did not when the reward was a shock in the posterior lateral hypothalamus. Only amphetamine produced striking resistance to extinction of self-stimulation behavior. The facilitation of self stimulation observed with chlordiazepoxide was independent of the rate of self-stimulation; it was rate dependent with amphetamine and scopolamine. Operant behavior with food reward was facilitated with amphetamine although consumption of food was depressed. Chlordiazepoxide had no effect on operant behavior for food reward but increased food consumption; scopolamine and diphenylhydantoin depressed responding. During extinction with food reward, amphetamine caused long lasting resistance to extinction; scopolamine had similar but transient effects; chlordiazepoxide had no effect, and diphenylhydantoin decreased resistance to extinction. The significance of these results are discussed in relation to the concept of arousal; the effects of the drugs seem to depend on their adding to or subtracting from the state of behavioral excitation of the animal induced either by self-stimulation or by hunger. It is concluded that the facilitation of moderate self-stimulators by amphetamine and scopolamine was due at least partially to their action on gross behavioral activity, that of chlordiazepoxide was not. 13 references. (Author abstract)

074937 Miller, F. P.; Cox, R. H., Jr.; Maickel, R. P. Lakeside Laboratories, Milwaukee, Wisconsin 53202 The effects of altered brain norepinephrine levels on continuous avoidance responding and the action of amphetamines. *Neuropharmacology (London).* 9(6):511-517, 1970.

A study is made of the effect of alpha-methyl-p-tyrosine (alpha-MT) on continuous avoidance behavior in the rat; and of the interaction between alpha-MT pretreatment -- with subsequent lowering of brain norepinephrine (NE) level --and the effects of D-amphetamine, p-chloramphetamine p-chloro-N-methylamphetamine. It was found that depressed NE levels in rat brain caused by administration of alpha-MT had differential effects on avoidance responding. A single dose of alpha-MT (100mg/kg, aqueous suspension, intraperitoneally) lowered the whole brain NE by 53% in 6 hr; this dose caused a significant reduction (-62%)in avoidance responding. In contrast, 4 doses of alpha-MT (150mg/kg, oil suspension, intraperitoneally) lowered brain NE by 39% at 6 hr after the last dose; these animals had a virtually normal rate of avoidance responding. This latter type of pretreatment with alpha-MT had little effect on the stimulation of avoidance responding evoked by p-chloroamphetamine or p-chloro-N-methylamphetamine. In contrast, the alpha-MT pretreatment changed the stimulatory action of a subsequent dose of D-amphetamine into a marked depression of avoidance responding. 17 references. (Author abstract modified)

075196 Harsh, John; Witters, Weldon L.; Yaremko, R. M. Ohio University, Athens, Ohio 45701 Effects of elymoclavine on wheel turning activity in mice. *Psychonomic Science.* 18(5):301-302, 1970.

The relationship between elymoclavine dosage level and general activity was explored. Groups of mice received elymoclavine, a drug chemically similar to lysergic acid diethylamide (LSD). Over 5 consecutive days, smaller dosage levels either enhanced or produced little change in wheel running activity, while higher dosages produced a decrement. 9 references. (Author abstract modified)

075197 Schuman, Marjorie; Isaacson, Robert L. University of Michigan, Ann Arbor, Michigan 48104 Penicillin-induced epileptogenic foci in the rat cortex. *Psychonomic Science.* 18(3):185-186, 1970.

This study describes some behavioral consequences of a penicillin induced cortical epileptogenic focus in the rat. Animals given a unilateral intracortical injection of penicillin in the posterolateral neocortex are more active than are control animals receiving an injection of saline into the same region. No differences were found in the learning and reversal of a spatial discrimination to final criterion performance, but there was a suggestion that the rate of learning might be different in the 2 groups. 7 references. (Author abstract)

075206 Thor, Donald H.; Hoats, David L.; Thor, Claudette J. Johnstone Training and Research Center, Bordentown, New Jersey 08505 Morphine induced fighting and prior social experience. *Psychonomic Science.* 18(3):137-139, 1970.

The possible effect of socialization during the administration interval upon group behavior during withdrawal from morphine was examined. Cohabitation during the morphine experience was anticipated to exert a restraint upon fighting during withdrawal. Groups of normally docile laboratory rats received morphine injections (to 600 mg/kg/day), placebo injections, or no injections under social or isolated conditions for 6 days. Postwithdrawal intragroup fighting was then monitored for 168 h by automated recording of loud vocalizations. Morphine treated groups spontaneously began sustained (30 h) fighting 3 days after terminal injections, with greatest fighting observed in the group receiving the drug under social conditions. 12 references. (Author abstract modified)

075234 Avery, David D.; Nance, Dwight M. Neuropsychology Laboratory, Department of Psychology, University of Houston, Houston, Texas 77004 Behavioral correlates of chemical stimulation in the cat thalamus. *Psychonomic Science.* 19(1):7-8, 1970.

The effects of adrenergic and cholinergic stimulation and blockage in the cat thalamus were investigated on food and water intake and operant responding. A facilitatory effect on responding with adrenergic stimulation and cholinergic blockage was observed. Cholinergic stimulation and adrenergic blockage lead to a deficit in response rate. Food intake increased with injections of nonadrenaline, and water consumption decreased with carbachol applications. Additionally, central applications of atropine sulfate reduced food intake. 15 references. (Author abstract)

075235 Chisholm, Drake C.; Moore, John W. University of Massachusetts, Amherst, Massachusetts 01002 Effects of chlordiazepoxide on the acquisition of shuttle avoidance in the rabbit. ***Psychonomic Science.*** **19(1):21-22, 1970.**

Rabbits injected with various dosages of chlordiazepoxide showed a decrement in the acquisition of a 2 way shuttle avoidance response. It is suggested that these results are not consistent with the notion that chlordiazepoxide reduces fear. 3 references. (Author abstract)

075236 Morgan, Laura L.; Schneiderman, Neil; Nyhan, William L. Department of Psychology, University of Miami, Coral Gables, Florida 33124 Theophylline: induction of self-biting in rabbits. ***Psychonomic Science.*** **19(1):37-38, 1970.**

A tentative animal model is presented for studying the self-mutilating behavior seen in children with an abnormality of purine metabolism. Each of 4 groups of rabbits was given a quarter normal diet and daily injections of saline or 46.0, 61.5, or 92.0mg/kg of anhydrous theophylline (1,3-dimethylxanthine). The major findings were that (1) the greatest number of self- biters were found in the 61.5mg/kg group, (2) mortality was directly related to drug dosage, and (3) the onset of biting occurred earliest with the highest dosage. 3 references. (Author abstract)

075237 Squire, Larry R. Albert Einstein College of Medicine, Bronx, New York 10461 Physostigmine: effects on retention at different times after brief training. ***Psychonomic Science.*** **19(1):49-50, 1970.**

Mice were given physostigmine 30 min, 1 day, 3 days, 7 days, or 14 days after brief training in a position habit, which normal animals forget within 14 days. The curve generated by the retention scores at these times was a miniaturization of the curve generated by previous studies using anticholinesterasesand prolonged training in a visual task. 10 references. (Author abstract)

075238 Glick, Stanley D. Albert Einstein College of Medicine, Bronx, New York 10461 Change in sensitivity to D-Amphetamine in frontal rats as a function of time: shifting of the dose-response curve. ***Psychonomic Science.*** **19(1):57-58, 1970.**

Three doses (0.5, 1.0, and 2.0mg/kg) of d-amphetamine and saline were administered to rats with frontal cortical ablations and to rats with sham operations during the first and sixth postoperative weeks. Locomotor activity of both groups of rats was measured following all injections. Hypersensitivity to d-amphetamine in the frontal rats was found to increase from the 1st to the 6th postoperative weeks. 2 references. (Author abstract)

075239 Martin Joan C; Becker, R. F. Duke University Medical School, Durham, North Carolina 27706 The effects of nicotine administration in utero upon activity in the rat. ***Psychonomic Science.*** **19(1):59-60, 1970.**

Holtzman male rat offspring whose mothers were injected twice daily throughout gestation with 3.0mg/kg nicotine differed little from saline injected control offspring on activity measures in the wheel. Offspring whose mothers were injected with the same dose of nicotine throughout gestation and the nursing period and offspring whose mothers received a 4% hypoxic episode throughout gestation were significantly more active than the control saline group. Differences were more extreme during the second week of testing than during the first. 20 references. (Author abstract)

075280 Suits, Evan; Isaacson, Robert L. University of Florida, Gainsville, Florida 32601 Behavioral effects: hippocampal destruction and scopolamine. ***Psychonomic Science.*** **18(1):9-11, 1970.**

Rats with sham, cortical, and hippocampal lesions were trained in 1 way and 2 way avoidance tasks while under the influence of scopolamine hydrobromide. The performance of the hippocampal lesion group was worse than that of the sham operate group on the 1 way task but better on the 2 way task. This demonstrates the efficiency of the lesion on drugged animals, despite the similarity of effects of both the lesions and the drug injections. 17 references. (Author abstract)

075282 Uyeno, Edward T. Stanford Research Institute, Menlo Park, California 94025 Lysergic acid diethylamide and a novel stimulus. ***Psychonomic Science.*** **18(1):52, 1970.**

The mean running time of rats injected with 0.016mg/kg of lysergic acid diethylamide (LSD 25) was not significantly different from that of others, administered saline solution. However, when a novel stimulus (hurdle) was presented in the runway, the mean running time of the experimental group was significantly longer than that of the control group. 5 references. (Author abstract)

075288 Browne, Lawrence; Judge, Fred; Kasper-Pandi, Phyllis. Psychology Department, Sir George Williams University, Montreal, Quebec, Canada Pentobarbital-induced state-dependent learning of one-way avoidance in mice. *Psychonomic Science.* 18(5):305-306, 1970.

Four groups of 8 albino mice were trained to avoid shock in a one way avoidance situation. Two groups received pentobarbital sodium during training and 2 groups received saline. One day after having reached the learning criterion, the mice received 1 test trial. Prior to the test trial, 2 groups received the same treatment they had received during training, and 2 received the other treatment. All 16 mice receiving the same treatment avoided on the test trial, whereas only 4 of the 16 mice receiving the change in treatment successfully avoided. Pentobarbital did not affect the rate of original learning of the one way avoidance response. 14 references. (Author abstract)

075314 Jackson, Donald E. Eastern Michigan University, Ypsilanti, Michigan Effects of 6-fluoro-N,N-diethyltryptamine (6-FDET) on selected rat behaviors. *Psychological Reports.* 26:139-142, 1970.

It has been shown that 6-Fluro-N,N-diethyltryptamine (6-FDET) produce the autonomic symptoms and mood changes characteristic of hallucinogens, but not perceptual and thinking disturbances. Hence it has been tested as an active placebo in clinical studies. In the absence of behavioral information about this drug, several studies were run to assess its effect on certain rat behaviors. It was found that 6-FDET exerts a fast acting, relatively short lived inhibitory effect on drinking and water motivated behaviors. No evidence was found to indicate the 6-FDET affects acquisition of conditioned suppression. 2 references. (Author abstract modified)

075316 Amit, Zalman; Stern, Muriel H. McGill University, Montreal, Province of Quebec, Canada Ambulatory behavior in the rat as a function of two methods of alcohol administration. *Psychonomic Science.* 18(5):273-274, 1970.

When alcohol was administered directly into the stomach, ambulation scores of rats in an open field apparatus were significantly higher than those following alcohol ingested by mouth, and higher following both methods of alcohol administration than after ingestion of water. This suggests that, while the pharmacologic properties of alcohol in general tend to reduce fear in the open field situation, eliminating the aversive taste of the alcohol increases its fear reducing effects. 6 references. (Author abstract)

075375 Huber, Helga; Longo, Nicholas. Universitat Dusseldorf, Dusseldorf, Germany The effect of Puromycin on classical conditioning in the goldfish. *Psychonomic Sciences.* 18(5):279-280, 1970.

Ninety six goldfish, divided into 6 groups, were trained in a classical retention deficit compared to the controls. In another experiment, 2 groups of 16 fish were given 4 days of training and were then injected immediately with puromycin or saline. There were indications of interference in this experiment also. These experiments are at variance with recent hypotheses that puromycin interferes with the consolidation stage of memory. 4 references. (Author abstract)

075399 Black, A. H.; Young, G. A.; Batenchuk, C. Department of Psychology, McMaster University, Hamilton, Ontario, Canada Avoidance training of hippocampal theta waves in flaxedilized dogs and its relation to skeletal movement. *Journal of Comparative and Physiolgical Psychology.* 70(1):15-24, 1970.

Two groups of dogs were trained to change the electrical activity of their dorsal hippocampus in order to avoid shock under flaxedil paralysis. One group was operantly reinforced for making hippocampal theta waves, and the other group for refraining from making them. Presentation of the discriminative stimulus following recovery from paralysis produced more theta responses and more skeletal activity in the first group than in the second. 22 references. (Author abstract)

075553 Reid, Larry D.; Wasden, Ronald E.; Courtney, Robert J. Bradley University, Peoria, Illinois 61606 Reinforcing limbic system stimulation and sodium amytal. *Psychonomic Science.* 18(1):47-48, 1970.

The discrete performance decrement, of rats in an alley maze, sometimes seen with 'positive' intracranial reinforcement was reduced, when the site of stimulation was the septal area, the dorsal hippocampus, or the amygdala, by administration of sodium amytal at fear reducing doses. 4 references. (Author abstract)

075559 Moran, Gary; Ahmad, S. Shamimuddin; Meagher, Robert B., Jr. Indiana University Northwest, Indianapolis, Indiana Adrenalin and

avoidance learning: partial replications. *Journal of Experimental Research in Personality.* 4:84-89, 1970.

Three partial replications of the Latane and Schachter finding that a weak adrenalin dosage facilitated avoidance learning in rats failed to reproduce the original finding. In experiment 1 adrenalin in saline glucose injected intraperitoneally resulted in significantly fewer avoidances. The same dosage in peanut oil administered subcutaneously in both experiments 2 and 3 resulted respectively in 40% fewer avoidances not specified and no difference from placebo comparisons. Behavior ratings of the rats' emotional, fearful, response to the conditioned stimulus in experiment 3 indicated significantly more emotionality in the adrenalin treatment. These findings simultaneously indicate poorer or equivalent avoidance learning and more emotionality in adrenalin aroused rats. Schachter's theory of emotions is supported but the reliability of avoidance learning as an indicant of emotionality is seriously questioned. 12 references. (Author abstract)

075579 Davison, M. C. Department of Psychology, University of Auckland, Private Bag, Auckland, New Zealand A choice technique to assess the effects of selective punishment on fixed-ratio performance. ***Journal of the Experimental Analysis of Behavior.*** **13(1):57-64, 1970.**

The emission of a fixed number of responses by rats was followed by food reinforcement. This fixed number could be accumulated in any way from two continuously available but mutually incompatible response classes, bar pressing, and not bar pressing for a fixed time period. A preference for one response class was arranged by specifying different maximum reinforcement rates for the two classes. Under selective punishment conditions, the preferred response occasionally led to both food and electric shock, while the nonpreferred response led only to food. Selective punishment effects were measured through changes in the preference to the two responses in the sequence. The actions of shock intensity, deprivation, the specification of the nonpreferred response, and three drugs were investigated. The results were broadly similar to the work reported by Dardano and Sauerbrunn (1964), who found localized increases in interresponse times before punished responses in fixed ratio schedules. Performance under this procedure was found to be stable and sensitive to each of the experimental variables examined. 22 references. (Author abstract)

075645 Harris, Wayne C.; Heistad, Gordon T. Department of Psychology, San Fernando Valley State College, Northridge, California 91324 Food-reinforced responding in rats during estrus. ***Journal of Comparitive and Physiological Psychology.*** **70(2):206-212, 1970.**

The effects of estrus on a food reinforced behavior known to be sensitive to deprivation level are presented. The relationship is explored between food reinforced response rate changes during the estrus cycle and ovarian hormone secretion. Female rats were food deprived and trained to press a lever for food on a schedule of reinforcement in which every tenth response was reinforced. Periodic response rate decreases suggestive of more rapid satiation were observed on days of maximum vaginal cornification and disappeared following ovariectomy. Estradiol injection 20 hr. before the experimental session produced a dose related response rate change in ovariectomized females, 25ug/kg producing a decrease similar to that associated with vaginal cornification. Since sexual receptivity and locomotor activity have not been reported 20 hr. after 25ug/kg of estradiol, the changes in food intake associated with maximum vaginal cornification appear to be the direct result of estrogen secretion and not secondary to heightened sexual motivation or increased activity. 15 references. (Author abstract modified)

075720 Davidson, Arnold B.; Cook, Leonard. Smith Kline and French Laboratories, 1500 Spring Garden Street, Philadelphia, Pennsylvania 19101 Comments on 'An effect of yeast RNA on behavior' (Mountford and Heslip). ***Psychonomic Science.*** **18(5):308, 1970.**

Comments are made on the disagreement of data from 2 laboratories on the effect of yeast ribonucleic acid on behavior. It appears that task specificity of yeast ribonucleic acid, evident in shock maintained tasks, is also evident in food maintained tasks. 2 references.

075788 Uyeno, Edward T. Department of Neurobiology, Stanford Research Institute, Menlo Park, California 94025 Effects of lysergic acid diethylamide on the maternal behavior of the rat. ***Journal of Psychology.*** **75:271-273, 1970.**

The effects of lysergic acid diethylamide (LSD-25) on the maternal behavior of rats were studied to test the hypothesis that LSD-25 will disrupt such behavior as represented by nursing behavior. Nine days after parturition, 20 male rats of the Wistar strain were matched according to their nursing behavior and assigned to an experimental and a control group. The experimental animals were injected intraperitoneally with .2mg/kg of LSD-25, while the control animals were given .9% saline solution. Fifteen minutes after the injection, they were administered a nursing test and observed for 3 hours. Most of the experimental animals did not start nursing until 10 hours after the initiation of the test, whereas all of the control animals began nursing within 5 minutes. The mean nursing time of the experimental group was significantly shorter than that of the control group, indicating that the administration of hallucinogenic compound disrupted the maternal behavior. 6 references. (Author abstract modified)

075829 Zumpe, D.; Michael, Richard P. Primate Behavior Research Centre, Institute of Psychiatry, Bethlem Royal Hospital Beckenham, Kent, England Redirected aggression and gonadal hormones in captive rhesus monkeys (Macaca mulatta). *Animal Behaviour (London).* 18:11-19, 1970.

Threat behavior characterized by being directed away from the sexual partner has been described in 5 oppositely sexed pairs of adult rhesus monkeys. It was established that threatening away did not occur in response to any external, environment stimulus, but did vary with the sexual activity of the pair. When male sexual interest in the female was high, male threatening away was more frequent and intense. Threatening away by females increased when female receptivity was increased either by subcutaneous injections or by brain inplants of estrogen. When female receptivity was reduced by progesterone administration, female threatening away also declined. It is argued that threatening away behaviour is redirected aggression and functions to consolidate the bonds between sexual partners. 32 references. (Author abstract)

05 TOXICOLOGY AND SIDE EFFECTS

074146 George, David J.; Wolf, Harold H. Department of Pharmacology, University of Utah, Salt Lake City, Utah 84112 Amphetamine toxicity and endogenous noradrenaline concentrations in isolated and aggregated mice *Journal of Pharmacy and Pharmacology (London).* 22(12):947-949, 1970.

In a letter to the editor, a study on amphetamine toxicity and endogenous noradrenaline concentrations in isolated and aggregated mice is reported. The relation between the enhanced toxicity of amphetamine in aggregated mice and noradrenaline depletion is unclear. An attempt was made to examine this relation. After an intraperitoneal injection of saline or (+)-amphetamine sulfate (30 or 100mg/kg) in aqueous solution (1 ml/100g), mice were either isolated or aggregated (3 per cage). Tissues were taken from nonsurvivors (within 3 h) and from surviving animals (3 h after injection). Noradrenaline contents of brains and hearts were determined. Results from animals treated with 100mg/kg of (+)-amphetamine show that death apparently is not due to a reduction of brain or heart noradrenaline below survival level. No obvious connection was found to exist between lethality and noradrenaline depletion in either brain or heart; differences in the degree of noradrenaline depletion may simply reflect the incluence of dose and duration of action of (+)-amphetamine. The time -dosage relationship is discussed. Results of the study suggest that the degree of depletion of endogenous stores of noradrenaline is not causally related to (+)-amphetamine lethality in isolated mice or the enhanced lethality in aggregated mice. 9 references.

075607 Brazelton, T. Berry. 51 Brattle St., Cambridge, Mass. 02138 Effect of prenatal drugs on the behavior of the neonate. *American Journal of Psychiatry.* 126(9):1261-1266, 1970.

Some of the intrauterine influences on neonatal behavior are outlined. Sex hormones used therapeutically in pregnancy may critically alter the genotype's sexual expression as well as its behavior. Dietary inadequancy in early fetal life may change the number and size of the infant's brain cells. Drug abuse by the mother produces chromosomal flaws as well as withdrawal symptoms in the newborn. Tranquilizers and premedications given mothers during delivery affect the neonate's initial weight gain and his response to nursing and early learning tasks. 34 references. (Journal abstract)

075840 Vedernikov, Y. P. Institute of Plant and Animal Ecology, Ural's Branch of USSR Acade-

myof Sciences, 8 Marta St., 202, Sverdlovsk, U.S.S.R. The influence of single and chronic morphine administration on some central effects of amphetamine and apomorphine. *Psychopharmacologia (Berlin).* 17:283-288, 1970.

With the aims of showing the influence of morphine on group toxicity and stereotypy produced by amphetamine and the influence of morphine on the stereotypy produced by apomorphine, a series of experiments were conducted on mice. It was found that acute toxicity of morphine did not differ in aggregated and ononaggregated animals, and that morphine in doses of 5, 10, 20, 40, and 80mg/kg (subcutaneously) did not significantly influence the amphetamine group toxicity in mice. Preliminary injection of morphine increased the occurrence of amphetamine stereotypy and prolonged the duration of stereotypy caused by amphetamine and apomorphine in intact rats, but failed to prolong the duration of the stereotype in rats tolerant to morphine. Some differences in the behavioral patterns after injection of amphetamine and apomorphine were observed. The development of tolerance to morphine affected differently the duration of the stereotypies produced by amphetamine and apomorphine. 12 references. (Author abstact modified)

06 METHODS DEVELOPMENT

073063 Boadle-Biber, Margaret C.; Hughes J.; Roth, R. H. Department of Pharmacology, Yale University, School of Medicine, 333 Cedar St., New Haven, Conn. 06510 Acceleration of noradrenaline biosynthesis in the guinea-pig vas deferens by potassium. *British Journal of Pharmacology (London).* 40:702-720, 1970.

In an experiment investigating methods of noradrenalin (NA) biosynthesis, it was found that increasing the concentration of potassium chloride (KC1) in Krebs -Henseleit bicarbonate solution enhanced the formation of l4C-noradrenaline (l4C-NA) from l4C-tyrosine in the guinea pig vas deferens. In 52 mM KC1 Krebs-Henseleit solution the specific activity of the newly formed l4C-NA was double that of controls. The rate of synthesis of l4C-NA from l4C-tyrosine was constant for up to 2 h in 52 mM KC1 Krebs-Henseleit solution and for 4 h in unmodified Krebs-Henseleit solution. The specific activity of l4C-tyrosine in the high KC1 treated vas deferens was 80% of that of control tissues. Thus the enhanced synthesis of 14C–NA in high KC1 Krebs-Henseleit solution did not arise from the increase in the specific activity of precursor. Removal of calcium ions or increasing the concentration of magnesium ions abolished the increase in synthesis of NA seen in high KC1 Krebs-Henseleit solution but left the basal rate of NA synthesis in unmodified Krebs-Henseleit solution unaltered. The spontaneous release of newly synthesized catecholamines (l4C-labelled) or tritiated noradrenaline (3H-NA) from vasa deferentia was increased in 52 mM KC1 Krebs-Henseleit solution. Removal of calcium ions reduced the increased efflux of newly synthesized amine in high KC1 media to that seen in unmodified Krebs-Henseleit solution. The efflux of 3H-NA was reduced to one-third of its former rate in the absence of calcium. High KCl Krebs-Henseleit solution caused a substantial contraction of the vas deferens which was not abolished by tetrodotoxin. Release of 3H-NA paralleled the contractile response, and was likewise unaffected by tetrodotoxin. 47 references. (Author abstract modified)

07 EARLY CLINICAL DRUG TRIALS

072421 Gutmann, Ludwig; Martin, James D.; Gutrecht, Jose A. Department of Neurology, West Virginia Medical Center, Morgantown, West Virginia L-Dopa therapy of Parkinson's disease (a review of the preliminary experience at West Virginia University). ***West Virginia Medical Journal.*** **66(4):109-111, 1970.**

Preliminary studies of L-dopa at the West Virginia University Medical Center demonstrate the effectiveness of the drug in the treatment of Parkinson's disease. Of the 16 subjects in the study, 8 patients, 4 moderately incapacitated and 4 severely incapacitated, demonstrated complete or almost complete alleviation of the symptoms of bradykinesia, lack of spontaneity and facial expression, and rigidity. The drug was less effective against tremor. Administration of the drug was done on the basis of a gradual increase starting with 750mg and increasing 250mg per day for approximately 3 weeks. This was usually administered as 4 to 6g per day in 4 doses. A variety of side-effects were observed, including agitation, depression, hallucinations, mental confusion, nausea and vomiting, postural hypotension and dyskinesias, the last being the most troublesome. Psychic side-effects were relieved by decreasing the dosage. Nausea and vomiting were alleviated by slowing the increase in medication dosage and by giving it at meals. 8 references.

08 DRUG TRIALS IN SCHIZOPHRENIA

072891 Popkowska, Natalia. Klinika Psychiatryczna AM, Abramowicka 2, Lublin, Poland /Clinical research into chronic incurable schizophrenia./ Badania kliniczne nad przewlekla nieuleczalna schizofrenia. ***Psychiatria Polska (Warszawa).*** **4(1):23-29, 1970.**

The reactivity of the vegetative system in a group of chronic schizophrenic patients resistant to any known therapeutic method and that of controls is examined. Respiration, heart activity, blood pressure, and pupillary reaction to light were recorded. Examinations were performed simultaneously under experimental conditions, prior to and during reaction to intramuscular injections of adrenaline, mecholyl, dihydroergotamine and atropine. A statistically essential difference was established in the reactivity of the group of chronic schizophrenics as compared with that of the mentally healthy controls. At the same time, all groups compared had an essentially similar run of the curves. In schizophrenics, the reactivity of the vegetative system was characterized by irregularity of deviations in the course of the different reactions to the tests. 22 references. (journal abstract modified)

072896 Marcjan, Kazimierz; Cwiertnia, Teresa; Wolak, Ewa. Klinika Psychiatryczna AM, Szpital Nowowiejski, Nowowiejska 27, Warsaw, Poland /Oxypertine in the treatment of chronic schizophrenia./ Wyniki stosowania oksypertyny w przewleklej schizofrenii. ***Psychiatria Polska (Warszawa).*** **4(1):63-67, 1970.**

Oxypertine (Win 18051-2, Forit) was administered to 27 patients (9 women and 18 men) ranging in age from 18 to 51 years; 24 of the patients had diagnoses of paranoid schizophrenia, 15 had marked symptoms of emotional deficiency and diminished activity, and 20 displayed delusions. Duration of illness had been from several months to about 20 years. Only 6 of the patients had been admitted for the first time; 21 had several admissions and had received treatment with neuroleptics, insuline, or electroconvulsant therapy. Oxypertine was applied orally in doses increased daily by 20mg to 40mg; maximal doses of 80mg to 320mg daily were used during 5 to 62 days. The mental state of 9 patients showed marked response consisting of improvement in activity, social adjustment and mood, and disappearance of delusions. Five patients showed only insignificant improvement, 11 did not respond, and 2 deteriorated. The only side effect observed in 9 patients was a mild Parkinson syndrome which was successfully controlled by means of Parkopan or other anti-Parkinson drugs. 14 references. (journal abstract modified)

072897 Romaszewska, Krystyna; Piotrowski, Andrzej. Klinika Psychiatryczna AM, ul. Nowowiejska 27, Warsaw, Poland /Evaluation of thiotixen in the treatment of schizophrenia./ Ocena skutecznosci tiotiksenu w leczeniu schizofrenii. ***Psychiatria Polska (Warszawa).*** **4(1):69-71, 1970.**

Thiotixen was used in the treatment of 23 schizophrenic patients (15 males and 8 females, ages ranging from 18 to 46 years) who had been ill

for an average of 4.5years. Thiotixen was administered orally in daily doses of 30mg to 40mg. Satisfactory results were observed in 16 patients. Apart from mild leukopenia in 1 case, no serious complications or side effects were noted. 4 references. (journal abstract)

074218 Holden, J. M. C.: Holden, U. P. St. Louis State Hospital Complex, St. Louis, Missouri Weight changes with schizophrenic psychosis and psychotropic drug therapy. *Psychosomatics.* 11(6):551-561, 1970.

Changes in weight patterns were studied in relation to psychopathology, diagnosis and age in a group of chronic schizophrenics treated over a prolonged period of time with placebo and chlordiazepoxide, thioridazine, alone and combined. Variations in appetite, motor activity or agitation were not consistently associated with changes in weight. Significant relationships were shown between increases in weight and improvement of psychotic symptomatology and decreases in weight and worsening of symptomatology. Various mechanisms to explain weight changes with psychosis are discussed, but the findings of this study suggest that changes in weight are an expression of the basic illness. An additional observation of the study was that weight changes were correlated inversely with hemoglobin and hematocrit shifts. These variations could also have been associated with variations in intensity of psychosis. Further studies will attempt to delineate the relationships between weight, psychopathology, EEG, and biochemical changes. 36 references. (Author abstract modified)

074625 Callaway, Enoch. Department of Psychiatry, University of California, San Francisco Medical Center, San Francisco, Calif. Arousal and schizophrenia. *Transactions.* 2(1):11-15, 1970.

It is argued that arousal is not the central issue in schizophrenia, a disorder characterized by an excessive instability of plans, although it plays an important role since arousal is increased by thought process disorder and, in turn, increases thought process disorder. It is suggested that cognitive instability rather than arousal is the common link between the various signs and symptoms that are seen in schizophrenia. Arousal may become a learned factor in each of the following 3 operations involved in changing plans: 1) a discrepancy between incoming data and image; 2) an executive system which operates to maintain a kind of consensus between the plans; and 3) prediction of an unpleasant outcome. The 2 major theories of schizophrenia which place arousal in a central and causal position, the inverted 'U' theory, and the response ceiling theory, are criticized. Experiments conducted with schizophrenics and controls involving both drugs commonly used in connection with mental disorders are discussed, giving arousal producing situations which illustrate that arousal theories are insufficient to explain schizophrenia. 18 references.

074874 Fleming, P.; Makar, H.; Hunter, K. R. Friern Hospital, London N. 11, England Levodopa in drug-induced extrapyramidal disorders. *Lancet.* 7684(2):1186, 1970.

Experimental findings have shown that levodopa does not improve drug induced extrapyramidal syndromes. This hypothesis was tested on 6 schizophrenic patients (3 subjects, 3 controls) who were taking fluphenazine decanoate and orphenadrine hydrochloride. The Ss taking levodopa were less withdrawn and more cheerful, with no significant change in extrapyramidal signs. It is concluded that although the mental state of the patients taking levodopa improved, the original hypothesis concerning extrapyramidal syndromes was confirmed. 2 references.

075212 Franzen, G. University of Lund, Department of Psychiatry II, St. Lars Hospital, 220 06 Lund, Sweden Plasma free fatty acids before and after an intravenous insulin injection in acute schizophrenic men. *British Journal of Psychiatry (London).* 116:173-177, 1970.

Plasma free fatty acids (plasma FFA), blood glucose, and pulse rate before and after an intravenous insulin dose, standardized according to body weight, were investigated in 28 male patients in a mental hospital: 14 patients were diagnosed acute schizophrenia and 14 were nonpsychotic patients. The 2 groups were compared both unmatched and matched for age, weight and duration of hospitalization prior to study. The psychotic patients generally showed higher FFA values than the nonpsychotics, and their heart rate was found to be higher at the beginning of the experiment. The schizophrenics tended to react to insulin with less hypoglycemia. It seems reasonable to suppose that increased activity in the autonomic nervous system in the schizophrenics is at least 1 basis for their increased FFA levels. 22 references. (Author abstract)

075227 Gittelman-Klein, Rachel; Klein, Donald F.; Blumberg, Arnold G.; Levenstein, Sidney. Research Department, Hillside Hospital, Glen Oaks, New York Relationships of the mecholyl test, premorbid asocial functioning and long-term outcome in schizophrenia. *The Journal of Nervous and Mental Disease.* 150(4):301-306, 1970.

This study addressed itself to the controversy whether magnitude of mecholyl response is related to premorbid characteristics and/or long-term outcome in nonchronic schizophrenics. It was found that in a group of 46 schizophrenics (17 to 57 years old) the ratings of premorbid asocial functioning were correlated with outcome. However, both of these patient characteristics were independent of the magnitude of a mecholyl induced drop in systolic blood pressure. Similar results were obtained when the schizophrenic sample was combined with 33 nonschizophrenic patients, thus suggesting that diagnostic variation among studies cannot account for contradictory results regarding the relationship between mecholyl response, process reactive schizophrenia, and long-term outcome. 27 references. (Author abstract)

075304 Birley, J. L. T.; Brown, G. W. Bethlem Royal Hospital and Maudsley Hospital, London, S.E.5, England Crises and life changes preceding the onset or relapse of acute schizophrenia: clinical aspects. *British Journal of Psychiatry (London).* 116:327-333, 1970.

From 123 schizophrenic patients, the first 50 were selected who had experienced an acute onset or relapse within three months of admission. Sixty percent of the patients had experienced at least 1 such an event during the 3 weeks prior to onset compared to an average of 23% during the 3 earlier 3 weeks periods. There were no significant differences by age, sex and diagnostic category between the 50 included and the 73 excluded patients. Within those who had experienced an acute onset, there were no differences between those who had and had not experienced any event in the final 3 weeks, except for certain depressive preoccupations in the former. Thirteen patients had stopped or reduced their phenothiazine medication. We conclude firstly that both life events and reducing or stopping phenothiazines contribute as precipitants of acute schizophrenia and secondly that the symptomatology of acute schizophrenia is largely unrelated to its precipitants. 23 references. (Author abstract modified)

075313 Simeon, Jovan; Fink, Max; Itil, Turan M.; Ponce, Danilo. Department of Psychiatry, New York Medical College, New York, N. Y. d-Cycloserine therapy of psychosis by symptom provocation. *Comprehensive Psychiatry.* 11(1):80-88, 1970.

The demonstration that cycloserine, an accepted therapeutic agent in the treatment of pulmonary tuberculosis, induces neurotoxic effects and behavioral changes at high doses suggested its therapeutic trial in a group of long-term severe mentally ill. Cycloserine was given to 10 patients in dosages from 1.0to 2.0g/day for 18 days to 16 weeks (mean, 50 days). While the therapeutic benefits of cycloserine treatment alone were poor, subsequent treatment with active psychotropic drugs resulted in marked behavioral improvement, with 6 patients discharged and 3 working in the hospital 6 months after study. This sequence of treatments (activation followed by psychotropic drug treatment) has been described as 'symptom provocation' therapy. Blood levels of cycloserine were related to the daily dosage and inversely related to weight. Blood levels below 45mcg/ml were accompanied by few behavioral changes, while levels above 65mcg/ml were accompanied by neurotoxic phenomena, suggesting a symptom - provocation range for cycloserine between 45 and 65mcg/ml. The electroencephalogram patterns with cycloserine were those of desynchronization, increased fast frequencies and increased variability. d-Cycloserine is an effective agent for symptom provocation with the unique advantage that an effective range can be defined by simple blood level estimations. 23 references. (Author abstract modified)

075321 Gottschalk, Louis A.; Gleser, Goldine C.; Cleghorn, John M.; Stone, Walter N.; Winget, Carolyn N. Department of Psychiatry and Human Behavior, College of Medicine, University of California at Irvine, Irvine, Calif. Prediction of changes in severity of the schizophrenic syndrome with discontinuation and administration of Phenothiazines in chronic schizophrenic patients: language as a predictor and measure of change in schizophrenia. *Comprehensive Psychiatry.* 11(2):123-140, 1970.

Seventy four hospitalized chronic schizophrenic patients were studied for 8 weeks to sequentially evaluate the effect of withdrawal and readministration of phenothiazine medication. The patients, in the age range 24-54, had been on some 1 phenothiazine derivative for at least the previous

6 months. For the first 4 weeks all patients were on placebo, while during the next 4 weeks half were on placebo and half were on thioridazine. Patients were assessed initially using the standardized Spitzer et al. mental status schedule and the Cattell 16 PF test. In addition, 2 or 3, 5 minute verbal samples were obtained from each patient in the initial pre-drug withdrawal week to assess the level of social alienation personal disorganization, hostility, and anxiety by the Gottschalk-Gleser method. Additional verbal samples were obtained twice weekly for the next 8 weeks and mental status schedule interviews were obtained at the end of 4 and 8 weeks. The theoretical and practical implications of the results are discussed. 34 references. (Author abstract modified)

075413 Held, Joan M.; Cromwell, Rue L.; Frank, E. T., Jr.; Fann, William E. Vanderbilt University School of Medicine, Nashville, Tennessee Effect of phenothiazines on reaction time in schizophrenics. *Journal of Psychiatric Research (Oxford).* 7:209-213, 1970.

The effect of phenothiazine or phenothiazine like drugs on simple motor reaction time (RT) was examined in 29 hospitalized schizophrenics. One group of 11 served as drug control patients and one group of 18 as placebo patients. A 2 week substitution of placebos for routine phenothiazine therapy did not appear to affect RT. 21 references. (Author abstract)

075421 Gardos, George; Finnerty, Richard J.; Cole, Jonathan O. Boston State Hospital, 591 Morton Street, Dorchester, Massachusetts 02124 Thiothixene and trifluoperazine in a step system. *Psychosomatics.* 11(1):36-40, 1970.

A double blind comparison study was carried out between thiothixene and trifluoperazine with 40 chronic, hospitalized schizophrenic patients for 12 months. In conjunction with the drug regime, there was a step system in which meaningful reinforcements were given for desired behavior. Results indicated that the Step System was effective in raising the level of functioning, enabling 6 patients to leave the hospital. The thiothixene group achieved a higher mean step rating in comparison with trifluoperazine. The difference in favor of thiothixene on the brief psychiatric rating scale (BPRS) emotional withdrawal and depressive mood, and on the nurses observation scale for inpatient evaluation retardation categories support the finding relating to the activating nature of the drug. The absence of reduction of BPRS Tension with thiothixene may also be a manifestation of a type of psychomotor activation. Side effects were less frequent in the thiothixene group, also. 7 references. (Author abstract modified)

075422 Sterlin, C.; Ban, T. A.; Lehmann, H. E.; Saxena, B. M. Hospital des Laurentides, L'Annonciation, Quebec, Canada The place of thiothixene in the treatment of schizophrenic patients. A systematic clinical study. *Canadian Psychiatric Association Journal (Ottawa).* 15(1):3-14, 1970.

On the basis of a pilot study carried out in 20 chronically hospitalized psychiatric patients, thiothixene was suggested to have psychotropic properties. The psychotropic properties of thiothixene were supported by the results of an uncontrolled clinical pharmacological study carried out on a total of 20 including 10 acute and 10 chronic, schizophrenic patients. In the same study antipsychotic properties were revealed. The antipsychotic properties of thiothixene were supported in 2 controlled clinical investigations in which the therapeutic effects of thiothixene were found to be significantly superior to an inactive placebo and comparable to at least 3 other antipsychotic drugs. The range of therapeutic activity, an almost exclusive effect on symptoms related to the psychological parameter of mental integration, associated with a beneficial effect on blunted affect, differentiates thiothixene from chlorpromazine, thioproperazine and chlorprothixene. In acute schizophrenic patients significant therapeutic changes with thiothixene were seen with four weeks. Twelve weeks is insufficient to produce statistically significant therapeutic changes with thiothixene in chronic schizophrenic patients. Side effects to thiothixene are minimal. 23 references. (Author abstract modified)

075423 Ananth, J. V.; Ban, T. A.; Lehmann, H. E.; Bennett, J. Douglas Hospital, Montreal 204, Province of Quebec, Canada Nicotinic acid in the prevention and treatment of methionine induced exacerbation of psychopathology in schizophrenics. *Canadian Psychiatric Association Journal (Ottawa).* 15(1):15-20, 1970.

In this placebo controlled crossover study nicotinic acid, in a fixed dosage of 3000 mg. a day, produced statistically significant improvement in chronic hospitalized schizophrenic pa-

tients. We were able to reproduce the clinical observations and results of previous workers; that is, the exacerbation of psychopathological symptoms by the combined administration of methionine and tranylcypromine. Nicotinic acid failed to prevent by prior administration or to relieve by subsequent administration, the methionine tranylcypromine induced exacerbation of psychopathology. This might have been due to the inadequate dosage of nicotinic acid given but the possibility of a toxic psychosis due to the metabolite, methionine sulfoximine, must be seriously considered. 23 references. (Author abstract)

075424 Straker, M. McGill University, Montreal, Province of Quebec, Canada Clinical experience with lithium carbonate. ***Canadian Psychiatric Association Journal (Ottawa).*** **15(1):21-27, 1970.**

Lithium carbonate is described in this paper as a mood normalizing drug, and recent literature is reviewed and summarized. Thirty one patients were treated with lithium in doses of 600-1200mg daily in order to attain a serum concentration of 0.5to 1.5meq./litre. This drug quickly arrested ongoing manic attacks in 11 patients and, when used prophylactically, has averted expected manic attacks in all 19 cases. Lithium, used in this way, also averted expected depressive reactions in 11 patients and modified such attacks in the remaining 8 patients. Where it did not prevent illness it appeared to facilitate the action of added antidepressive drugs, while not being a potent antidepressive drug when used alone. Lithium also showed promising results in the treatment of 6 patients with recurrent depressions and for 5 patients diagnosed as having schizoaffective reactions. Careful studies are required to establish whether toxic effects on various organs will emerge after long usage, but lithium carbonate must be regarded as a remarkable addition to the existing list of psychiatric drugs. A full exploration of its clinical application is warranted. 23 references. (Author abstract)

075429 Yaryura-Tobias, Jose A.; Wolpert, Arthur; Dana, Lawrence; Merlis, Sidney Division of Research, Central Islip State Hospital, Central Islip, New York Actions of L-dopa in drug induced extrapyramidalism. ***Disease of the Nervous System.*** **31(1):60-63, 1970.**

The purpose of this investigation was to evaluate the action of L-dihydroxyphenylalanine (L-DOPA) in drug induced extrapyramidal symptoms and to study behavioral changes during administration. Chronic schizophrenic patients with drug induced extrapyramidal signs and who were completely or very well controlled on standard antiparkinson medication were the subjects. Deterioration in patient status limited the study to 4 subjects. The results from this small sample confirm earlier reports that L-DOPA is not the agent of choice in the treatment of drug induced parkinson syndrome. One case report is presented to illustrate some of the problems encountered. 23 references. (Author abstract modified)

09 DRUG TRIALS IN AFFECTIVE DISORDERS

072429 No author. Author address not given Prophylactic lithium. ***British Medical Journal (London).*** **No. 5721:479-480, 1970.**

Double-blind studies on bipolar manic-depressives and on recurrent depressive patients by Baastrup et al. and by Melia strongly support the prophylactic effect of lithium in recurrent affective disorders. This effect may not be evident until 6 to 12 months after the initiation of lithium treatment, and occurring relapses should be treated with appropriate tranquilizers while maintaining the lithium dosage. Lithium administration should be started at low dosages to minimize side-effects and gradually increased to 600 to 1600mg/day, and serum lithium levels should be followed. At the first indication of toxicity (vomiting, ataxia, coarse tremor, fasciculation, marked drowsiness, slurred speech or confusion) treatment should be stopped and hemodialysis initiated. Lithium should never be given to patients with cardiac or neural decompensation or with impaired water or electrolyte balance, and should only be used during pregnancy when there is a high risk of recurrent illness. 11 references.

073706 Walcher, W. Psychiatrisch-Neurologische Klinik der Universitat, Graz, Austria /Clinical investigation with the butyrophenone derivative 'Buronil'./ Klinische Untersuchungen mit dem Butyrophenonderivat 'Buronil'. ***International Pharmacopsychiatry (Basel).*** **4(1-2):59-66, 1970.**

Comparative clinical results on the application of 'Buronil,' a butyrophenone compound is reported. The expectations based on pharmacologic experiences with the drug were confirmed. Because of the overall sedating effect with preservation of specific antipsychotic action and

reduced side-effects on the vegetative and extrapyramidal systems, the compound occupies a position midway between the long acting and the broad applicable neuroleptic drugs, while potency of action is increased in both these directions compared to Haloperidol. The compound is especially suited for treatment of symptoms of agitation with disorientation such as occurring in manic states, delirium tremens and psychoses of exogenous type. Here, daily doses of 300 to 600mg have to be used. In cases of Korsakow and amentia, postpartum psychoses, etc.,150 to 300mg usually suffice. Indications and effectiveness of Buronil correspond roughly to those of Haloperidol in cases of acute and chronic schizophrenia. 13 references. (author abstract)

073708 Schwingenheuer, J. Landeskrankenhaus Warstein, Fachkrankenhaus fur Psychiatrie, D-4788 Warstein, Germany /Initial and interval treatment of acute psychoses with intravenous injection of Inofal./ Die initial-und intervallbehandlung akuter Psychosen mit intravenoser Applikation des Inofal. *International Pharmacopsychiatry.* 4(1-2):92-97, 1970.

Over a 7 month period, a total of 400 intravenous Inofal injections were given to 67 patients. Six to 9 injections per patient were given to all of them within 3 to 4 days. Indications were manifold psychiatric diseases with states of tension and excitation, hyperactivity, tendencies to aggressiveness, anxiety, agitated depression, urging restlessness, troubles of adjustment and troubles of sleep. With intravenous administration marked effects on initial damping and sleep induction were observed. Compared with oral administration Inofal given intravenously proves to have markedly higher neuroleptic potency; the ratio between intravenous and oral administration is about 1 : 2, i.e. single doses or 150 mg daily of intravenously administered Inofal correspond to single oral doses of 100 mg and daily oral doses of about 300 mg. The advantages of an initial treatment of acute psychoses or interval treatment of exacerbating psychiatric diseases are both a fast onset of action and good local and general compatibility. At onset of treatment and especially with not pretreated patients the content of the ampoules (50 mg Inofal) should be injected slowly within 2 to 3 min. After individual testing of the respective patients, the injection time can be reduced to about 1 minute. With all age groups (15 to 80 years) the same fast onset of action was observed and the intravenous administration of Inofal gave very favorable results. Few side-effects were observed. 6 references. (author abstract modified)

074926 Klerman, Gerald L. Harvard Medical School, c/o Bulfinch 3, Massachusetts General Hospital, 2 Fruit Street, Boston, Massachusetts 02114 Drugs in the treatment of depression. *World Journal of Psychosynthesis.* 4(11):31-34, 1970.

The use of drugs in the treatment of depression is discussed, with a review of 3 classes of specific antidepressants: the psychomotor stimulants, the monoamine oxidase inhibitors, and the tricyclic antidepressants. The place of phenothiazine, sedative hypnotics, and minor tranquillizers in the treatment of depression are described; and the treatment of some of the complications of depression, particularly mania, are also discussed. 11 references.

075410 Greenspan, Kenneth; Schildkraut, Joseph J.; Gordon, Edna K.; Baer, Leslie; Aronoff, Michael S.; Durell, Jack. New York State Psychiatric Institute, Columbia Presbyterian Hospital Center, 722 West 168th Street, New York, New York Catecholamine metabolism in affective disorders--III. MHPG and other catecholamine metabolites in patients treated with lithium carbonate. *Journal of Psychiatric Research (Oxford).* 7:171-183, 1970.

The urinary excretion of catecholamines and their metabolites was studied longitudinally in 9 patients with histories of manic-depressive disorders. The patients were studied first during a 'pretreatment period' in which placebo was administered, and subsequently during a 'treatment period' in which lithium carbonate was administered. During the 'pretreatment period', excretion varied amongh the 3 groups of patients, hypomanic, normothymic, and agitated depressed, dependent on the clinical state of the patient. For the group as a whole, the excretions of normetanephrine and metanephrine decreased significantly when lithium carbonate was administered. The changes in the excretion of the catecholamines and the deaminated o-methylated metabolites 3-methoxy-4-hydroxymandelic acid and 3-methoxy-4-hydroxyphenylglycol (MHPG), however, appeared to be more consistently related to changes in clinical state than to administration of lithium carbonate, although a direct action of lithium carbonate cannot be excluded.

While definitive interpretation of the data is not possible, it is suggested that, in the patients with agitated depressions, the decrease in MHPG excretion may reflect decreased central noradrenergic activity; evidence of increased adrenomedullary activity and, in some cases, increased peripheral sympathetic activity is provided by the elevated levels of epinephrine and metanephrine and, in some patients, norepinephrine and normetanephrine. The data further suggests that patients with hypomania have increased peripheral sympathetic and adrenomedullary activity, and possibly increased central noradrenergic activity. 35 references.

075428 Earle, Brian V. 12 First Avenue, Ilion, New York 13357 Thyroid hormone and tricyclic antidepressants in resistant depressions. ***American Journal of Psychiatry.*** **126(11):1667-1669, 1970.**

A study of 25 retarded depressed patients who previously responded inadequately to tricyclic antidepressants has been conducted. Thyroid hormone was administered to the group while the antidepressant therapy was continued. Fourteen patients showed an excellent response to the combination. It is concluded that thyroid hormone potentiates the effects of the tricyclic antidepressants to some extent, but that there is need for further study in this area. 3 references. (Journal abstract modified)

075430 Spring, Gottfried; Schweid, Daniel; Gray, Carl; Steinberg, Joel; Horwitz, Marc. Department of Psychiatry, University Hospitals of Cleveland, Cleveland, Ohio 44106 A double-blind comparison of lithium and chlorpromazine in the treatment of manic states. ***American Journal of Psychiatry.*** **126(9):1306-1310, 1970.**

A double blind technique using stringent diagnostic criteria and a standardized method of evaluation for comparing lithium carbonate and chlorpromazine in the treatment of acute mania has been applied in this research. Lithium carbonate, at a dosage of 1,800mg daily, was found to be effective in the treatment of acute manic states. However, when compared with chlorpromazine, no significant difference between the 2 drugs was noted. In regard to the prophylactic effect of lithium, the data presented indicate that this question is still unresolved. It is believed that the method used here will render more useful data on the drug as research continues. 10 references. (Journal abstract modified)

10 DRUG TRIALS IN NEUROSES

073707 Molcan, J.; Motylova, A.; Polak, L. Mickiewiczova 13, Bratislava, Czechoslovakia /A contribution to the depressive disorder pharmacotherapy by the combination of amitriptyline and perphenazine./ Ein Beitrag zur Pharmakotherapie depressiver Storungen mittels der Kombination von Amitriptylin und Perphenazin. ***International Pharmacopsychiatry.*** **4(1-2):77-81, 1970.**

Preliminary observations indicated that a combination of 2 drugs would be beneficial in cases of depressive disturbances, where the atypical excitative symptoms were present or where a psychokinetic stimulation during the cure with amitriptyline was manifested. Twenty cases of endogenous, reactive, neurotic, schizophrenic or arteriosclerotic depressive syndromes were followed. The drug was administered in a mixture and the ratio of ingredients was changed according to the psychopathologic state of the patient. The rations did not surpass 225 mg of amitriptyline and 96 mg of perphenazine per day. The therapeutic effect was evaluated according to rating scales. Results revealed that the desired effect of the mixture was obtained even in those cases where former cure with only amitriptyline or other antidepressive drugs did not lead to any improvement. In 3 cases it was nevertheless necessary to substitute with imipramine. The necessity of psychopharmacotherapy has been substantiated, which, on the basis of psychopathological status, tries to influence all the respective syndromes of the illness. It proved true mostly in cases of depression with atypical excitative symptoms and with schizo-affective psychosis. 6 references. (author abstract)

074130 Downing, R. W.; Rickels, K. Department of Psychiatry, Pa. Division, Philadelphia General Hospital, Philadelphia, Pennsylvania Patient personality and demographic factors as predictors of early response to psychotropic drug treatment. ***Comprehensive Psychiatry.*** **11(6):568-575, 1970.**

In a drug treatment situation the response of the patient early in treatment is of considerable importance. The quality of the patient's preliminary treatment response plays a critical role in determining both patient and physician set, and hence influences the atmosphere in which medication effects take place. In the present preliminary study, a stepwise multiple regression procedure was employed in an attempt to derive orienting in-

formation about factors affecting early treatment response. Factors were sought which would be related to the treatment response of predominantly lower socioeconomic neurotic outpatients after 2 weeks of treatment with either placebo or one of several antidepressants or antianxiety agents. The Ss were 76 anxious and/or depressed neurotics, of whom 20 were given chlordiazepoxide, 22 received meprobamate, 21 were treated with minor miscellaneous drugs, and 13 were given a placebo. Analyses for the study were made on data derived both from interviews and from several psychometric instruments. Results from the study appear either consistent enough across predictors or sufficiently in accord with independent findings to lend further credence to the predictive efficacy of an inadequate syndrome, an adequate syndrome, and of acute, relatively mild presenting symptomatology. 20 references.

075388 Dull, Theodore A.; Tuzel, Ilhan H.; White, Robert F. Department of Medical Research Hoffmann-La Roche Inc., Nutley, New Jersey The value of worsening rates in psychiatric clinical trials. ***Psychosomatics.*** **11(1):50-54, 1970.**

The clinical improvement and worsening rates for Nobrium, phenobarbital and placebo are 2 indices which demonstrate the superiority of Nobrium, a benzodiazepine derivative, for the treatment of agitation, anxiety-tension, depression and insomnia. A report is presented on the significance of determining patient worsening rates in double-blind crossover clinical trials. It is felt that the determination of the worsening rate in clinical trials of psychotropic agents is an additional dimension for determining the efficacy of the test agent. This report contains analysis and discussions of 34 double-blind crossover studies, where a psychotropic agent, Norbrium, was compared to placebo in 27 studies and to phenobarbital in 7 studies. 2 references. (Author abstract modified)

075415 Rickels, Karl; Gordon, Paul E.; Jenkins, B. Wheeler; Perloff, Milton; Sachs, Ticu; Stepansky, William. Department of Psychiatry, University of Pennsylvania, Philadelphia, Pennsylvania Drug treatment in depressive illness: amitryptyline and chlordiazepoxide in two neurotic populations. ***Diseases of the Nervous System.*** **31(1):30-42, 1970.**

A controlled clinical trial of amitriptyline, chlordiazepoxide, a combination of both drugs, and placebo was conducted with 243 neurotic depressed clinic and general practice patients. Both populations differed significantly in social class and its related variables. Data were analyzed using a factorial covariance approach, testing for drug, population, and drug x population interaction effects. At 2 as well as 4 weeks, not only consistent significant drug effects, but also several population and drug x population interaction effects were observed. The data may be summarized as follows: the 3 active agents always produced significantly more improvement than placebo, and a consistent pattern emerged with the drug combination producing the most improvement, followed closely by chlordiazepoxide and amitriptyline; and while the 3 active drugs did not differ significantly from each other, a strong trend for such difference, particularly between drug combination and amitriptyline, frequently existed. Drug combination and amitriptyline caused more side effects than chlordiazepoxide and placebo. Main population effects indicated that middle social class general practice patients improved significantly more than low social class clinic patients; and several interaction effects pointed out that both populations differed primarily in their response to active drugs and not to placebo. Possible explanations of the results are discussed. 22 references. (Author abstract modified)

075425 Stancer, Harvey C.; Furlong, F. Wayne; Godse, D. D. Clarke Institute of Psychiatry, Toronto, Canada A longitudinal investigation of lithium as a prophylactic agent for recurrent depressions. ***Canadian Psychiatric Association Journal (Ottawa).*** **15(1):29-40, 1970.**

Twenty one patients with recurrent endogenous depressions were treated with lithium carbonate for periods up to 2× years. Although depressions did not recur in 6 of 8 patients with nonperiodic disorders who were on lithium, the treatment did not reduce the frequency of exacerbation in 11 of 13 periodic disorders. Urinary measurements of sodium, potassium, 17-ketosteroids, hydroxy steroids and lithium in several of the patients did not help to differentiate them by their reaction to lithium. It is concluded that the notion of lithium as an effective prophylactic agent against recurrent depressions, based on decreased frequency or increased interval between episodes, is not supported by this study. 20 references. (Author abstract)

075426 Angrist, Burton M.; Gershon, Samuel; Levitan, Stephan J.; Blumberg, Arnold G. Neuropsychopharmacology Research Unit, Department of Psychiatry, New York University School of Medicine, New York, New York Lithium-induced diabetes insipidus-like syndrome. ***Comprehensive Psychiatry.*** **11(2):141-146, 1970.**

Two cases are reported who developed a diabetes insipidus like syndrome during the course of treatment with lithium salts of psychiatric disorders. Symptomatology was characterized by excessive thirst, high urine volumes, low urinary specific gravity and inability to concentrate urine, even under conditions of water deprivation. Both failed to concentrate urine in response to either the infusion of hypertonic saline or to an injection of pitressin. A paradoxical diuresis following infusion of hypertonic saline was noted. Although no clinical evidence of hypokalemia was seen, urinary excretion of potassium was diminished in 1 case and total body potassium was shown to be decreased by total body counting procedures. In both cases, this syndrome resolved only after lithium had been discontinued for up to 3 weeks. It is suggested that the mechanism for this renal impairment is based on a temporary hypokalemic nephropathy. 10 references. (Author abstract)

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

072465 Fisher, Robert G. Department of Surgery, University of Oklahoma Medical Center, Norman, Oklahoma New aspects in the therapy of Parkinsonism. ***Journal of the Oklahoma State Medical Association.*** **63(9):412-416, 1970.**

The drug L-dopa has proven to be an efficient therapy for Parkinsonism. Recognition should be stressed that this is not a cure all. Best results with L-dopa and adjunct medications occurred in those patients who had successful bilateral thalamotomies. The drug is expensive; it is hoped that the pharmaceutical concerns will eventually reduce their prices. Eighty nine patients were treated for an average followup of 1 year without fatality or serious accident although side-effects such as nausea, vomiting and dyskinesias have occurred in many. A course of therapy that may be of help to physicians in the State of Oklahoma has been suggested and aid with this regimen may be obtained from the neurologists in this state. 5 references. (author abstract modified)

072787 Symington, Aileen. Moditen Clinic, London, Ontario, Canada New in psychiatry: moditen injectable therapy and follow-up care. ***Canadian Nurse (Ottawa).*** **66(1):21-24, 1970.**

The services of a unique psychiatric outpatient clinic, primarily concerned with fluphenazine enanthate therapy, are reviewed. Called the Moditen therapy, fluphenozine enanthate is an extremely effective therapy that rapidly permits patients to return to life outside the hospital. The drug therapy requires close medical supervision, however, and thus the purpose of the special clinic and its staff of psychiatrists, social workers, and nurses. Continued clinical care provides the medication plus supportive interviews and intensive psychotherapy. Results of Moditen therapy have been most encouraging. The drug itself, in use since 1965, is a member of the phenothiazine family and is manufactured to be effective over a 2 or 3 week period. It reduces hostility, anxiety, agitation, and hyperactivity. Adverse physical and behavior side effects occur, but are usually controlled by adjusting dosage.M

072895 Galuszko, Pawel; Wroblewska-Smoczynska, Janina. Klinika Chorob Psychicznych AM, ul. Debinki 7, bud. 25, Gdansk 6, Poland /Clinical study of efficacy of amizepine./ Wlasne doswiadczenia kliniczne nad amizepina. ***Psychiatria Polska (Warszawa).*** **4(1):57-61, 1970.**

Effects of treatment with amizepine (POLFA) in patients with various forms of epileptic attacks are presented. Fifty patients were administered amizepine for 10 weeks to 7 months in daily doses of 400mg to 900mg. Total improvement or remission of attacks was obtained in 24 cases, reduction of attack in 17 cases, and no improvement in 9 cases. The efficacy of the drug was found to be greatest in the treatment of temporal lobe attacks (psychomotor, psychosensory, and dysthymic), less in generalized clonic attacks, and absent in petit mal attacks. Amizepine can be used both for outpatient and inpatient treatment; side effects in the form of dizziness or drowsiness occur vary rarely. 8 references. (journal abstract modified)

074732 Finer, Morris J. Hines, Illinois Habituation to chlordiazepoxide in an alcoholic population. ***Journal of the American Medical Association.*** **213(8):1342, 1970.**

Six hundred thirty alcoholic patients, for whom chlordiazepoxide hydrochloride was prescribed, have demonstrated a high degree of habituation to

the drug. Chlordiazepoxide is used for relief of anxiety and tension and is frequently used in managing alcoholic patients. A syndrome is described, associated with abstinence from chlordiazepoxide, which may persist as long as 4 weeks. Patients in the population reported were well aware of their dependency as evidenced by their frequently pleading for that specific drug. Evidence cited suggests that diazepam is similar in effectiveness to chlordiazepoxide and much less habituating.

075332 Merlis, Sidney; Sheppard, Charles; Collins, Lois; Fiorentino, Diane. Central Islip State Hospital, Central Islip, N. Y. 11722 Polypharmacy in psychiatry: patterns of differential treatment. ***American Journal of Psychiatry.*** **126(11):1647-1651, 1970.**

Five hundred patients, 125 men and 375 women, were randomly selected from a group of 1,350 patients treated with combinations of psychoactive medications. Each patient had been on his treatment combination for a minimum of 30 days prior to admission to the study and was considered relatively stabilized before initial assessment. A team of raters, who had no knowledge regarding treatment regimens, interviewed and recorded manifest pathology on the 18 item brief psychiatric rating scale (BPRS) and judged degree of mental illness on a 7 point scale. The patients were then divided into 3 groups. One group was abruptly taken off all active medications for psychiatric symptoms, with placebo being substituted for their original therapy. A second group had 1 active medication discontinued and a placebo substituted. The third group remained on their usual treatments. All patients were rerated after a 30 dayperiod. Analysis of covariance for multiple covariants was applied to measure significance of differences in behavioral rating scores. Included as control variables were age, duration of hospital stay, degree of mental illness, total pathology, and first assessment cluster scores. The data, analyzed separately by sex, demonstrated that polypharmacy is often, particularly in males, an inadequate treatment procedure. Some implications and inferences were discussed. 5 references. (Author abstract)

075584 Sikes, James C.; Sikes, Sweeney C. College Street Hospital, Inc., 685 College Street, Macon, Georgia Lithium carbonate treatment in psychiatry. ***Diseases of the Nervous System.*** **31(1):52-55, 1970.**

This is a report on an informal investigation of the use of lithium carbonate in the treatment of primarily affective disorders. Sixty five patients were treated with 1 of 2 oral preparations of lithium carbonate for various periods of time in hospital and outpatient settings. The group included 14 patients with diagnosed manic-depressive reactions, 10 schizophrenic reactions, and 41 psychotic depressive reactions. The results of the study indicate that lithium carbonate is a very useful adjunct in psychiatric therapy. It often enhances other agents such as tranquilizing and antidepressent drugs. The margin of safety is wide but only when adequate studies prior to and during treatment are carried out. These studies include serum lithium and sodium levels, thyroid function tests and neck measurements. Lithium carbonate has been shown to add greatly to the treatment of affective disorders, particularly manic-depressive illnesses, but it is also useful in other depressions as well as in schizophrenic illnesses with affective components. 26 references. (Author abstract modified)

075819 Roukema, Richard W.; Emery, Louise. Ridgewood, N. J. Megavitamin therapy with severely disturbed children. ***American Journal of Psychiatry.*** **127(2):249, 1970.**

A letter to the editor reports a pilot project which was carried out with 19 children who were severely emotionally disturbed (autism, schizophrenia, severe anxiety, chronic brain syndrome, grand mal epilepsy) in an attempt to determine whether megavitamin therapy B3 would prove beneficial. Therapy was conducted in a day school. After 1 year of treatment no significant change in the children's motor or mental behavior was noticed. 2 references.

075837 Faragalla, F. F.; Flach. F. F. Department of Psychiatry, The New York Hospital, Cornell Medical Center, 525 East 68th Street, New York, New York 10021 Studies of mineral metabolism in mental depression. I. The effects of imipramine and electric convulsive therapy on calcium balance and kinetics. ***Journal of Nervous and Mental Disease.*** **151(2):120-129, 1970.**

Calcium metabolic studies in 9 emotionally depressed patients before and after electric convulsive therapy (ECT) or administration of a course of imipramine showed that treatment was associated with marked decrease in serum calcium concentration in most patients. The possible relationship of the finding to the phenomenon of

depression has been discussed. Treatment with ECT in all patients and with imipramine in most was associated with improved calcium retention manifested by a shift toward positive balance. In most of these cases this resulted from increase in net absorption from the gut and decreased urinary calcium excretion. Calcium kinetic studies indicated that the increased retention due to electric convulsive therapy was caused by decreased bone resorption. In 3 out of 4 patients treated with imipramine, the increased calcium retention was associated with increased bone formation, which was marked in 2 patients and less marked in 1. The possible use of imipramine for treating osteopenia of unknown origin where bone formation is low has been suggested. 28 references. (Author abstract)

12 PSYCHOTOMIMETIC EVALUATION STUDIES

073852 Kurland, Albert A. Department of Mental Hygiene, State of Maryland The therapeutic potential of LSD: its adjunctive use in psychotherapy. *Medical Tribune.* 11(37):15, 1970.

The unique potency and dramatic psychotropic effects of LSD have resulted in numerous investigations attempting to delineate their specific characteristics and possible application in treatment. Investigative endeavors seeking to apply these in the psychotherapeutic setting have resulted in the structuring of 3 different techniques: psycholyptic psychotherapy, uncovering the unconscious material that can be psychodynamically analyzed with much time devoted to psychotherapy before, during, and after actual drug sessions; psychodelic chemotherapy, placing its major emphasis on the drug sessions itself during which psychotherapy may or may not be carried out; and psychodelic - peak therapy, achieving of a peak or transcendental experience after which careful attention is paid to integrating the experiences gleaned from emerging insights. The latter technique has been under intensive scrutiny in clinical studies being conducted with alcoholics, neurotics, character disorders, narcotic addicts, and in terminal cancer patients. Future research might produce new substances having brief or longer periods of activity as compared to LSD as well as yielding psychotropic effects. These substances and the intense emotional states they elicit may be useful in resolving depression, overcoming a sense of inertia or apathy, or providing aging individuals with increased sense of comfort, zest, or fulfillment.

074782 Rodin, Ernst A.; Domino, Edward F.; Porzak, James P. 951 E. Lafayette, Detroit, Michigan 48207 The marihuana-induced 'social high': neurological and electroencephalographic concomitants. *Journal of the American Medical Association.* 213(8):1300-1302, 1970.

Ten healthy, male freshman medical students who admitted to long term marijuana use are studied after attaining their usual 'high' by inhaling marijuana in the laboratory. Baseline histories were obtained 3 weeks before the experiment. Electroencephalograms (EEGs) were monitored continuously as each subject smoked, an interview was taped, mental status assessed, and neurological examination, vibratory sense determination, and Bender-Gestalt tests were repeated. Few changes were noted, although a slight but significant shift toward slower alpha frequencies on the EEG was observed. No evidence of illusions, hallucinations, or paranoid thinking was found, but thinking was subtly changed. The Bender-Gestalt test scores worsened, falling into an abnormal range after marijuana smoking. Vibratory sense showed some improvement. Pleasure derived from the drug is thought to be a result of a decrease in critical judgment and loosening of inhibition. 4 references.

074858 Gilder, S. S. B. author address not given Tread softly on my LSD. *Canadian Medical Association Journal (Toronto).* 103(13):1347, 1970.

Arguments over the merits and demerits of LSD are summed up. Several psychiatrists report cases of delayed psychotic episodes due to the drug, suggest that its long-term use may contribute to psychiatric morbidity, and hold that it should not be used in psychiatric treatment. Other psychiatrists think the connection between the drug and the psychosis is tenuous and that one should hesitate to discard any promising psychiatric drug on anecdotal evidence.

075191 Gaston, E. Thayer; Eagle, Charles T., Jr. University of Kansas, Lawrence, Kansas The function of music in LSD therapy for alcoholic patients. *Journal of Music Therapy.* 7(1):3-19, 1970.

In the laboratory, controlled use of lysergic acid diethylamide (LSD) can induce mental distortions resembling natural psychosis. This study obtained quantative data concerning the function of

music in LSD therapy and of alcoholics. Since musical structure is not distorted, it affords a link to reality. Types of music most beneficial to each patient is determined by his past experience. 20 references.

075290 Faillace, Louis A.; Vourlekis, Alkinoos; Szara, Stephen. Department of Psychiatry, Johns Hopkins University School of Medicine, Baltimore, Maryland Hallucinogenic drugs in the treatment of alcoholism: a two-year follow-up. *Comprehensive Psychiatry.* 11(1):51-56, 1970.

Twelve chronic alcoholic patients who were treated with hallucinogenic drugs were evaluated 2 years after drug treatment. Of the 12 subjects, three were relatively stable, 8 were drinking or hospitalized at the time of followup, and 1 subject was lost to followup. Of the 3 improved, only 2 could be considered to have benefited from the drug. From our data, the use of hallucinogenic drugs in the treatment of alcoholism appears to be of limited value. 17 references. (Author abstract)o

075841 Hollister, Leo E.; Moore, Frances; Kanter, Saul; Noble, Ernest. Veterans Administration Hospital, 3801 Miranda Avenue, Palo Alto, California 94304 Delta 1-tetrahydrocannabinol, synhexyl and marijuana extract administered orally in man: catecholamine excretion, plasma cortisol levels and platelet serotonin content. *Psychopharmacologia (Berlin).* 17:354-360, 1970.

Measurements of catecholamine excretion, plasma cortisol and platelet serotonin concentration were done in the course of experiments in which human volunteers were given sizable oral doses of delta'-tetrahydrocannabinol (THC), synhexyl or marijuana extracts. A transient rise in epinephrine excretion was observed following THC but seemed best explained by the anticipatory stress of the experiment or the rapid onset of unfamiliar symptoms. A decreased turnover of catecholamines or a shift in the degradative pathways of catecholamines from the oxidative to the reductive route was suggested by the decrease in vanilmandelic acid excretion following synhexyl. Plasma cortisol was unchanged except in the presence of clinically obvious psychological distress on the part of the patient. Platelet serotonin was unchanged. The lack of major effects of marijuana like drugs on these and other clinical measurement of stress corroborates the clinical observation that drugs of this type seem to be less stressful than the usual psychotomimetics. The pronounced euphoriant and sedative effect of marijunana may ameliorate the stress of the psychotomimetic experience. 9 references. (Author abstract)

13 MECHANISM OF ACTION - PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

072587 Steidinger, J.; Schmid, E. I. Medizinische Klinik der Medizinischen Akademie, 2400 Lubeck, Kronsforder Allee 71/73, Germany /Studies on the metabolism of 7-chloro-1,3-dihydro-3-hydroxy-5 -phenyl-2H-1,4-benzodiazepin-2-one./ Untersuchungen uber den Stoffwechsel von 7-Chlor-1,3-dihydro-3 -hydroxy-5-phenyl-2H-1,4-benzodiazepin-2-on. *Arzneimittel-Forschung (Aulendorf).* 20(9):1232-1235, 1970.

For 7-chloro-1,3-dihydro-3-hydroxy-5-phenyl-2H-1,4-benzodiazepin -2-one (oxazepam, Adumbran) a new quantitative determination withthin layer chromatographic isolation and measurement of fluorescence on the sorption layer is described. In patients with cirrhosis, the oxazepam recovery of 21% of the dose applied within 48 hr is lower than that of 36% in subjects with normal liver function. The glucuronide - bound part of oxazepam in the urine of normal persons amounts to a mean of 90.8%, that in cirrhosis patients to 85.4%, on the average. The small difference in the rates of glucuronidation was statistically secured. 52 references. (author abstract)

073710 Heinemann, L. G.; Itil, T. M. Missouri Institute of Psychiatry, 5400 Arsenal Street, St. Louis, Missouri 63139 Quantitative EEG changes during high and low dosage fluphenazine hydrochloride treatment. *International Pharmacopsychiatry.* 4(1-2):43-52, 1970.

During a treatment program for 19 chronic schizophrenic patients with 2 dosages levels of fluphenazine (average low dosage of 17.4mg and high dosage of 60 mg) in the course of 5 months, after a 2 month placebo period, EEG's and clinical evaluations using 2 rating scales were obtained at regular intervals. Three methods of EEG evaluation were applied and compared: spectral density analysis, using an analog frequency analyzer; a digital computer program for period analysis and average amplitude, and visual rating of 10 items on a 5 point scale. Alpha activity increased from placebo to low dosage and high dosage periods, the difference reaching statistical

significance in the analog frequency analysis and in the visual rating of synchronous alpha groups. Similarly, the topographical extension of rhythmical alpha activity increased significantly, whereas the occurrence of sleep episodes decreased in the visual evaluation. Beta activity increased from placebo to low dosage, but later decreased at high dosage. This pattern was seen in all 3 methods and reached statistical significance in the digital computer period analysis measures. A number of clinical ratings indicated thatthe patients' improvement occurred at a statistically significant level, but no correlation between clinical symptoms and EEG measurements could be demonstrated at a significant level. 22 references. (author abstract)

073770 Bechtereva, N. P.; Kambarova, D. K.; Matveyev, Yu. K. Otdel prikladnoy neyrofiziologii Instituta eksperimental'noy meditsiny Akademii meditsinskikh nauk SSSR, Leningrad, U.S.S.R. /Functional characteristic of the links of the brain control system for mental and motor functions in man./ Functsional'naya kharakteristika zven'yev mozgovykh system kontrolya psikhicheskikhi dvigatel'nykh funktsiy u cheloveka. *Fiziologicheskii Zhurnal SSSR imeni I. M. Sechenova (Moskva).* 56(8):1081-1097, 1970.

Impulse activity pattern of neuronal assemblies in deep brain structures was studied during motor and psychological tests presented either under ordinary conditions or after neurotropic drug administration. Areas were discovered in various brain structures in which characteristic reproducible impulse activity pattern was observed during the performance of psychological and/or motor tests. The characteristic reproducible pattern of the impulse activity could occur in various nuclei or in different zones of the same nucleus in response to movement of either contralateral limb alone or the limbs of both sides. Neurotropic drugs (dezeril, L-DOPA), when applied, changed the background frequency and the pattern of impulse activity during motor and psychological tests up to disappearance or, on the contrary, appearance of the characteristic reactions in areas where, prior to drug administration, they were either clear or absent. The present study ascertained a few links of the brain systems of the mental and motor control and their properties, and demonstrated the dynamics of flexible links of these systems under influence of changes in the internal state of the brain. 21 references. (author abstract)

075112 Mellerio, Francoise. Hopital Fernand-Widal, Rue du Faubourg Saint-Denis 200, F-75, Paris 10, France /Principal electroencephalographic changes observed during acute intoxication by neuroleptics./ Principales modifications electroencephalographiques observees au cours des intoxications aigues par neuroleptiques. *Acta Psychiatrica Belgica (Bruxelles).* 70(6):730-742, 1970.

In a study of 140 cases of isolated or predominant acute intoxication by phenothiazines, it is shown that these drugs induce slight EEG disturbances, which are much less pronounced than those induced by other toxic substances (administered for similar clinical purposes). The effects of associated drugs on cerebral electrogenesis are reviewed, as well as the effects of different phenothiazines on epileptic features, on the activation of EEG patterns and on hypothermia. Notwithstanding the fact that neuroleptics can only be usefully studied through animal experiments and that EEG pattern does not give a clear picture of their action, it is nevertheless believed that EEG is useful for the study of acute drug intoxication. EEG patterns differ after the administration of drugs belonging to different pharmacological groups, despite the fact that bioelectric patterns have no specificities. It seems that from a practical point of view, EEG provides elements of appreciation which help to formulate valid prognoses. 16 references. (Journal abstract)

075161 Bradshaw, John L. Monash University, Victoria, Australia Pupil size and drug state in a reaction time task. *Psychonomic Science.* 18(2):112, 113, 1970.

Changes in pupil size were monitored during the performance of an auditory reaction time task, under 3 drug conditions: normal, alcohol, and amphetamine. Under amphetamine, baselinedilations were increased, but neither the shape or amplitude of the pupillary response peak nor the obtained RT were otherwise affected. With alcohol, the average pupillary baselines were no lower than normal, but the response peaks were considerably flattened and RT increased. Long warning foreperiods resulted in fractionally faster performance than short. 6 references. (Author abstract)

075274 Kopell, Bert S.; Wittner, William K.; Lunde, Donald; Warrick, Gudrun; Edwards, David. Department of Psychiatry, Stanford University Medical Center, Stanford, California 94305 Cortisol effects on averaged evoked potential,

alpha-rhythm, time estimation, and two-flash fusion threshold. ***Psychosomatic Medicine.*** **32(1):39-49, 1970.**

Eighteen normal male subjects, each serving as his own control, were tested with acute cortisol and placebo intravenous infusions on separate days. Previous studies have shown that enhancement of the amplitude of the averaged evoked potential by random flashes reflects selective attention. Cortisol administration was accompanied by a significant decrease in this enhancement. It is therefore hypothesized that cortisol may be acting to decrease the subject's ability to attend differentially to visual stimuli. Cortisol significantly increased the latency of the averaged evoked potential resulting from flashes when the subject attended to flashes. Several measures reflecting time perception were significantly changed by cortisol in a direction comparable with a slowed internal clock, produced intervals were longer with the drug. Cortisol produced no changes in 2 flash fusion threshold, mood adjective check list scores, and alpha rhythm. 37 references. (Author abstract)

075300 Frosch, William A. author address not given Psychoanalytic evaluation of addiction and habitation. ***Journal of the American Psychoanalytic Association.*** **18(1):209-218, 1970.**

The panel considered a number of aspects of the problems of addiction and habitation. There is evidence that experiences at early stages of development as well as social and cultural influences contribute to the behavior patterns of drug abuse. The pharmacologic properties of the agents used must also be considered. Addicts share certain needs and coping mechanisms. There are also significant differences in ego and superego functioning which help determine the choice of the addictive substance and the quality of their adaptation. It makes a difference whether the substance is used as a means of coping with the problems of daily living or of avoiding them. Discussion of the therapeutic approach suggests that the main goal is to help the drug user attain or regain healthy narcissism: a sense of dignity based on real relationships and accomplishments in place of spurious feelings of omnipotence supplied by the drug use. The most important therapeutic tool seems to be a continuing relationship with a helping person who provides supporting ego and superego functions. A group situation combining confrontation and acceptance is also important. (Author abstract modified)

075412 Solomon, George F.; Rubbo, Sydney D.; Batchelder, Elaine. Department of Psychiatry, Stanford University School of Medicine, Stanford, California Secondary immune response to tetanus toxoid in psychiatric patients. ***Journal of Psychiatric Research (Oxford).*** **7:201-207, 1970.**

Schizophrenic patients have been reported to have diminished antibody response to administered antigens. Such relative immunologic incompetence, if present, might relate to the various dysproteinemias, autoimmune phenomena and lymphocyte abnormalities reported in conjunction with schizophrenic illnesses. We administered tetanus toxoid to 13 schizophrenic and 13 nonschizophrenic mentally ill veteran inpatients and to 6 normal controls. The schizophrenic patients did not differ in their secondary immunologic response from our normal controls or from normals reported by others, but the nonschizophrenic patients showed a somewhat impaired immunologic response not reaching statistical significance. Phenothiazine drugs showed no effect on antibody response. 26 references. (Author abstract)

075470 Herzberg, Brenda; Coppen, Alec. Mental Health Research Fund, Area Laboratory, West Park Hospital, Epsom, Surrey, England Changes in psychological symptoms in women taking oral contraceptives. ***British Journal of Psychiatry (London).*** **116:161-164, 1970.**

The premenstrual syndrome first described by Frank (1931) includes a number of psychological and physical symptoms appearing in the week before menstruation and relieved by the onset of the period. The etiology is still obscure. Progesterone (Greene and Dalton, 1953; Rees, 1953) and more recently oestrogenprogestogen preparations used as oral contraceptives (Mears, 1965) have been reported to be effective therapy. In view of the likely relationship between endocrinological changes and the premenstrual syndrome, a decision was made to investigate the effect of oral contraceptives on these symptoms. The present work also examines some of the psychological side effects of these preparations. 10 references

075471 Marcotte, David B.; Kane, Francis J.; Obrist, Paul; Lipton, Morris A. University of North Carolina School of Medicine, Chapel Hill, North Carolina Psychophysiologic changes accompanying oral contraceptive use. ***British Journal Psychiatry (London).*** **116:165-167, 1970.**

There have been many studies on the effects of oral contraceptive hormonal agents, though relatively few have concerned themselves with the possible adverse emotional reactions accompanying their use. To date, 7 women have had psychotic episodes in temporal association with drug use, 1 patient having reported 2 such episodes. Four of these 7 women had a history of severe postpartum disturbance in the past, and 2 others had previous psychiatric illness. There have been reports of varying incidence of depression, anxiety, increased or decreased sexual desire and relief of premenstrual tension. Data from a pilot double-blind study of 1 combination oral contraceptive are presented. 19 references

14 MECHANISM OF ACTION - BEHAVIORAL

072585 Jovanovic, U. J.; Liebaldt, G. P. Universitats-Klinik und Poliklinik, Fuchsleinstrasse 15, 8700 Wurzburg, Germany /Clinical, clinico-chemical and brain-bioelectric tests of a combination of hexobendine, etamivan and hydroxyethyltheophyllin./ Klinische, Klinisch-chemische und hirnbioelektrische Prufung einer Kombination aus Hexobendin, Etamivan und Hydroxyathyltheophyllin. *Arzneimittel-Forschung (Aulendorf).* 20(9):1223-1230, 1970.

Thirty mostly elderly patients of a psychiatric hospital ward were treated with a combination of hexobendine, etamivan and hydroxyethyltheophyllin (Instenon). Clinical symptoms, clinicochemical findings and bioelectric brain activity were examined and the correlation of these parameters was calculated. The clinical psychopathological symptoms improved quickly with Instenon therapy so that the patients could be dismissed from the hospital after 39.2days or 5.6weeks, on the average. Clinicobiochemical findings which had been abnormal or pathological in most patients before treatment were not influenced unfavorably by therapy with Instenon. Normalization or at least tendency to normalization was observed by the end of the therapy. The brain activity, which in 19 out of 30 patients was seriously changed before therapy and moderately so in the remaining 11, returned to normal during therapy or showed improving tendency at least. The correlation coefficients between improved and normalized symptoms are relatively high and thus positive. 15 references. (author abstract)

072588 Mikus, P. 291 Westerstede, Kreiskrankenhaus, Germany /Effects of different sedatives on self-ratings depending on sex and personality./ Die Wirkungen verschiedener Sedativa auf die Selbsteinschatzung der Befindlichkeiten in Abhangigkeit von Geschlecht und Personlichkeit des Beurteilers. *Arzneimittel-Forschung (Aulendorf).* 20(9):1235-1238, 1970.

In a double-blind experiment applied to 133 students according to a variance analytic design, the efficiency of different sedatives was examined by the subjects rating their own feelings. These feelings were recorded by an adjective checklist, which proved to be a reliable and valid instrument along with other psychological variables, namely the stability of mood and activity. The subjects' sex was introduced as variance analytic factor. The pharmacological factors were the drugs 7-chloro-2-methylamino-5-phenyl-3H-1,4-benzodiazepine -4-oxide hydrochloride (chlordiazepoxide), phenylethyl-barbituric acid (phenobarbital) and a drug in test called HS-2314 (1-N-methylpiperidyl -4'-2-phenyl-3,4-dihydronaphthaline). These drugs were tested against placebo effect. Only the variable 'activity' of the adjective checklist showed significant differences between the drugs: chlordiazepoxide stabilized the individually felt activity, whereas all the other drugs (including placebo) diminished the subjects' activity as a result of the experiment's boredom. 12 references. (author abstract)

072825 Minde, Klaus K.; Weiss, Gabrielle C. Montreal Children's Hospital, Montreal, P. Q., Canada The assessment of drug effects in children as compared to adults. *Journal of Child Psychotherapy (London).* 9(1):124-133, 1970.

It is difficult to obtain valid knowledge of drug effects on children; however, the special problems of drug research with children are being recognized. The behavior of children and its modification can be realiably assessed at school; standardized academic and social expectations facilitate intergroup comparisons and the selection of untreated control groups. Children are more responsive than adults to small fluctuations in immediate environment, and change attributed to drug effect must be carefully evaluated against these effects. One study finds that children above 10 years respond differently to some medications than younger children. Suggestions for the evaluation of drug effects in pediatric psychopharmacology are offered, since fundamental con-

tributions in understanding drug therapy can result from such research. 32 references.

073886 Tinklenberg, J. R.; Melges, F. T.; Hollister, L. E.; Gillespie, H. K. Departments of Psychiatry and Medicine, Stanford University School of Medicine, Stanford, California Marijuana and immdiate memory. *Nature (London).* 226:1171-1172, 1970.

Measured doses of tetrahydrocannabinol (THC) were given to 8 students to simulate the effects of marijuana on immediate memory. The THC was extracted from marijuana and quantitative calibrations were contained in doses of 20mg, 40mg, and 60mg. The dosages were in the range which invariably produces clinical effects approaching those of psychotomimetic drugs such as lysergide. A placebo was composed from an extract of marijuana with cannabinoids removed. The subjects, who were fasting, and who had previously smoked marijuana but only about once a month, received their doses in randomized order unknown to subject or testers. Tests were conducted in an austere laboratory, before the drug was given, and at 1.5hours, 3.5hours, and 5.5hours afterward. Subjects were required to repeat, either forwards or backwards, a series of random digits read by the experimenter at a rate of 1 per second. No significant differences between dose levels was seen, indicating that a small dose impairs immediate memory but a larger dose does not significantly augment the impairment. Observations confirmed the findings of others, that impairment in immediate memory from marijuana intoxication does not follow a smooth time function but is episodic, brief in duration, and not always under volitional control. The cognitive impairments induced by THC also involved intermittent lapses in attention. Usually the cognitive changes abated in 3 to 5 hours, although some subjects described residual impairment up to 24 hours later. Similar intermittent defects in memory may contribute to various types of behavioral disorders including acute psychoses. 8 references.

074135 Lader, M. H.; Mathews, A. M. Institute of Psychiatry, University of London, London, England Comparison of methods of relaxation using physiological measures. *Behaviour Research and Therapy (Oxford).* 8(4):331-337, 1970.

The utility of physiological measures as indicators of treatment response to several methods of relaxation is investigated. The effects of a single injection of methohexitone sodium or saline were monitored in 18 anxious patients using forearm blood flow, heart rate, skin conductance and fontalis electromyogram. The physiological changes were compared to those when the patients listened to tape recorded instructions to relax or listened to a tape of neutral content. No differences were found between the treatments except for an increase in skin conductance fluctuations following the injection. A marked dose dependent tachycardia was induced by methohexitone sodium. 10 references. (Author abstract modified)

074938 Bowers, M. B., Jr. Department of Psychiatry, Yale University, New Haven, Connecticut Cerebrospinal fluid 5-hydroxyindoles and behavior after L-tryptophan and pyridoxine administration to psychiatric patients. *Neuropharmacology (London).* 9(6):599-604, 1970.

The 5-hydroxyindoles of cerebrospinal fluid and behavior of psychiatric patients are observed after the administration of L-tryptophan and pyridoxine to investigate the relationship between behavioral change and increase in 5-hydroxytryptamine metabolism in the central nervous system. L-Tryptophan (2-8g/day) and vitamin B6 (100mg/day) were administered for 1 to 3 weeks to 15 newly admitted psychiatric inpatients who were diagnosed as depressive or schizophrenic and who had taken no other psychotropic medications for at least a week. Measurements for cerebrospinal fluid 5-hydroxyindoles, the brief psychiatric rating scale (BPRS), and sleep were made before and at the termination of the L-tryptophan regimen. For the patient group as a whole, increases in cerebrospinal fluid 5-hydroxyindoles correlated significantly with decreases in certain individual BPRS items, with the total sickness score, and with the total items score. In depressives, neither depressive symptoms nor insomnia were remarkably ameliorated by these doses of L-tryptophan and B6. Schizophrenic patients as a group seemed more responsive to the L-tryptophan regimen than depressives. 15 references. (Author abstract modified)

075103 Saarma, J.; Saarma, M. Department of Psychiatry, Tartu State University, Tartu, U.S.S.R. Evaluation of the therapeutic effect of neuroleptics upon the higher nervous activity in schizophrenia. *Acta Psychiatrica Belgica (Bruxelles).* 70(6):753-761, 1970.

In a sample of 127 chronic schizophrenics the action of chlorpromazine, trifluoperazine, haloperidol, levomepromazine and a combination of chlorpromazine with trifluoperazine was investigated by means of a complex of tests. It was found that the excitatory process in cortical mechanisms is favorably influenced most of all by trifluoperazine and levomepromazine, the internal inhibition by levomepromazine and the equilibrium of nervous processes by levomepromazine and trifluoperazine. The action of drugs upon cortical nervous processes is to be taken into account to warrant individually the most efficacy of treatment. 4 references. (Author abstract)

075111 Fazio, C.; Rossi, R. Clinica delle malattie nervose e mentali dell'Universita di Roma, Roma, Italy /Problems presented by neuroleptic therapy in Italy./ Problemes poses par la therapie neuroleptique en Italie. ***Acta Psychiatrica Belgica (Bruxelles).*** **70(6):743-752, 1970.**

Certain sociological and epidemiological aspects of psychopharmacology, and particularly those concerning the use of neuroleptics in Italy, are examined. The problem of the attitude toward neuroleptic therapy and with the organizational modalities of these therapies with their social and technical implications is discussed. They emphasize the characteristic phenomenon of underdosage, linked to insufficient medical and social assistance in the matter of followup, and also to the more frequent use of the neuroleptics as sedatives and anxiolytics rather than as specific antipsychotic drugs. In the light of the Italian experience, it is believed that neuroleptic therapy can only fulfill its action very imperfectly in the absence of a modern and well structured organization of psychiatric assistance permitting a longitudinal followup of the patients. 16 references. (Journal abstract)

075115 Bobon, Daniel P. Clinique psychiatrique universitaire, Rue St-Laurent 58, B-4000 Liege, Belgium /The neuroleptics: an interdisciplinary attempt of synthesis, based on 'The Neuroleptics.'/ Les neuroleptiques: essai interdisciplinaire de synthese, a propos de l'ouvrage 'the Neuroleptics.' ***Acta Psychiatrica Belgica (Bruxelles).*** **70(6):661-675, 1970.**

'The Neuroleptics' contains the conclusions of 11 Round Table Conferences at which 120 well known specialists from 22 countries (among them the USSR and Japan) tried to establish the state of present knowledge on the antipsychotic drugs and to open up new paths in understanding them. The first 11 chapters are entitled histological and molecular biochemistry, neurophysiology, pharmacology, toxicity and side effects in man and in the laboratory animals, animal behavior, clinical and experimental electroencephalography, classification of mental disorders, clinical methodology, definition and classification of neuroleptics, therapeutic problems, epidemiological and sociological aspects. A twelfth chapter is devoted to the W. H. O. Reference Centre Network for information on psychotropic drugs. The work is of further interest because of the 400 or so bibliographic references and its index of the generic or registered names of 800 neuroleptics. (Journal abstract)

075315 Lobb, Harold, Kaplun, Jack. Department of Psychology, University of Western Ontario, London, Ontario, Canada Protection of GSR conditioning by dextroamphetamine. ***Canadian Journal of Psychology (Toronto).*** **24(1):15-26, 1970.**

d-Amphetamine (0.175mg/kg) or placebo capsules were given to human adults on 2 successive days in a factorially designed study of galvanic skin response (GSR) acquisition and extinction. Subjects performed a phi phenomenon task during sessions with tone and electric shock as the conditioning stimuli. The drug prevented habituation of conditioned GSRs during acquisition trials, and when given next day it prevented extinction. However, the capacity of this dosage to offset GSR habituation to the tone in a control group was relatively weak, and no influence was discernable on GSRs to shock, levels of skin resistance, or phi phenomenon response. 15 references. (Author abstract)

075362 Shader, Richard I., Grinspoon, Lester. Department of Psychiatry, Harvard Medical School, Boston, Massachusetts The effect of social feedback on chronic schizophrenic patients. ***Comprehensive Psychiatry.*** **11(2):196-199, 1970.**

Feedback on patterns of social interaction was given to chronic schizophrenic patients at their weekly ward community meetings for a period of 4 weeks. This feedback produced a significant decrement in aloneness (from an initial level of 80% to 72%) relative to the initial prefeedback period. Isolation had returned to the initial prefeedback level six months later at which time a replication of the feedback procedures again produced a similar aloneness decrement. No dif-

ferences were observed between drug (phenothiazine) and placebo patients. 15 references. (Author abstract)

075771 Gruzelier, J. H.; Corballis, M. C. Birkbeck College, University of London, London, England Effects of instructions and drug administration on temporal resolution of paired flashes. ***Quarterly Journal of Experimental Psychology (Cambridge, Eng.).*** **22:115-124, 1970.**

One source of ambiguity in 2-flash fusion threshold (TFT) experiments, the concept of threshold, is the particular concern of the present study on the effects of instructions and drug administration on temporal resolution of paired flashes. Sixteen male alcoholics were shown pairs of light flashes separated by intervals ranging from 0 to 100 msec.,and judged whether there were 1 or 2 flashes. TFT was raised by administration of promazine hydrochloride, a tranquilizing drug, and was higher for strict than for lenient instructions. Signal detection analysis showed that the drug reduced sensitivity but did not affect criterion, while instructions altered criterion placement without changing sensitivity. 23 references. (Author abstract modified)

075793 Dews, P. B. Laboratory of Psychobiology, Department of Psychiatry, Harvard Medical School, 25 Shattuck St., Boston, Mass. 02115 Drugs in psychology: a commentary on Travis Thompson and Charles R. Schuster's behavioral pharmacology. ***Journal of the Experimental Analysis of Behavior.*** **13(3):395-406, 1970.**

This is a discussion of the relatively new field of behavioral pharmacology. The first textbook in this field, Behavioral Pharmacology by Travis Thompson and Charles R. Schuster, is evaluated and termed a reflection of the relative immaturity of the field. Support is given to Thompson and Schuster's decision to exclude 4 areas of drug effects from the book: motor capabilities; sensory functions; motivation, and learning. The concept of 'big effects' presented in the book is discussed as well as interpretation of selectivity and susceptibility criteria on these. Mechanism of drug action is reviewed. 15 references.

15 TOXICOLOGY AND SIDE EFFECTS

072508 Thompson, Richard A.; White, Joseph C., Jr.; Echols, Charles L., Jr. Division of Neurology, Barrow Neurological Institute, St. Joseph's Hospital and Medical Center, Phoenix, Arizona The effects of L-dopa therapy in Parkinson's disease. ***Arizona Medicine.*** **27(7):5-10, 1970.**

A study was undertaken to evaluate the adverse effects of levodopa on 154 patients. The most serious of these effects were anorexia, nausea, vomiting, asthenia, and weight loss. Twenty nine percent of patients dropped out of the study because of these symptoms. Involuntary movements were also a problem but could usually be prevented by adjustment of dosage. Fifty eight percent of patients experienced some degree of hypotension, but only 5 experienced syncope. Other adverse effects on the cardiovascular system were rare. Two patients developed hallucinations. Other possible psychic manifestations included agitation and depression. Only transient leukopenia was noted in 9 patients. Transient abnormalities in blood chemistries were noted as follows: BUN, 17 patients; SGOT, 4 patients; LDH, 1 patient; alkaline phosphatase, 1 patient. There were 6 deaths among the patient group. The relationship of levodopa to their death is questionable. 6 references. (author abstract)

072890 Wasik, August. Klinika Psychiatryczna AM, ul. Kraszewskiego 25, Wroclaw, Poland /Isonicotinic-acid-hydrazide (INH)-induced mental disorders in the course of lung tuberculosis treatment./ Zaburzenia psychiczne wywolane hydrazydem kwasu izonikotynowego (INH) w przebiegu leczenia gruzlicy pluc. ***Psychiatria Polska (Warszawa).*** **4(1):17-22, 1970.**

Mental disorders in the course of lung tuberculosis treatment with isonicotinic acid hydrazide (INH) are described in 37 patients. In group 1, deliriamentive syndromes (17 patients) prevailed for 1 to 4 weeks, preceded by preminitory symptoms chiefly including emotional and vegetative changes of the type of ergotropic system stimulation. Four patients simultaneously showed symptoms of polyneuritis. In the clinical picture of group 2 (8 cases), delusions prevailed; this made differentiation from schizophrenia necessary. The disorders lasted an average of 3 to 6 weeks. Groups 3 and 4 consisted of patients with pseudoneurotic disorders and such intensification of characteropathic traits that there was a need for psychiatric consultation. Alcoholism, a past history of lesion to the central nervous system, or advanced age were predisposing factors to psychoses, particularly deliriamentive. Of the neuroleptics used, thioridazine and sparine proved ef-

fective. Reduction or withdrawal of hydrazide was found indicated only in group 1; after remission of acute psychotic symptoms, hydrazide was reincluded using concurrent neuroleptic protection. 23 references. (journal abstract modified)

072893 Klosinska, Bozena; Wierzbicki, Tadeusz. Ul. Aleksandrowska 159, Lodz, Poland /Mental disorders caused by phenmetrazine abuse./ Przypadki zaburzen psychicznych pod wplywem naduzywania fenmetrazyny. ***Psychiatria Polska (Warszawa).*** **4(1):45-47, 1970.**

Two cases of mental disorders following excessive use of phenmetrazine in daily doses of 5 to 10 tablets during several months are described. The subjects involved had been using the drug for slimming purposes, and had never before shown any psychotic signs. After withdrawal of phenmetrazine, and treatment, both patients returned to normal. Because of such toxicity, the compound should be used with special caution. 5 references. (journal abstract modified).

073711 O'Connell, Ralph A. Psychiatric Research Division, St. Vincent's Hospital and Medical Center, New York, New York 10011 Leukocytosis during lithium carbonate treatment. ***International Pharmacopsychiatry (Basel).*** **4(1-2):30-34, 1970.**

An intermittent leukocytosis was observed in an outpatient population of 25 patients receiving lithium carbonate treatment for the prophylaxis of recurrent affective disorders. This periodic leukocytosis was statistically significant when compared to pretreatment levels and to a control group. The rise in leukocytesis attributed to an increase in neutrophiles. It is hypothesized that a change in steroid metabolism accounts for the leukocytosis and and increased glucose tolerance. 6 references. (author abstract modified)

073788 Gol'dovskaya, I. L. Institut psikhiatrii Akademii Meditsinskikh Nauk SSSR, Moscow, U.S.S.R. /Ophthalmological studies of patients receiving psychotropic preparations./ Ob oftal'mologicheskom obsledovanii bol'nykh, poluchayushchikh psikhotropnyye preparaty. ***Zhurnal Nevropatologii i psikhiatrii imeni S. S. Korsakova (Moskva).*** **70(5):759-762, 1970.**

An ophthalmological study of 3000 patients receiving different psychotropic preparations was conducted. Complications of the visual organs were seen in 7 patients (0.23 percent). In 1 case there was an aminazine pigmentation of the lens which did not, however, affect the visual function. One patient, during aminazine treatment, displayed a dimness in the anterior capsule of the lens (on the basis of uveitis encountered in the past). During treatment with antidepressive drugs, 3 patients receiving MAO inhibitors had a changed color perception and a temporal hemianopsia to green colors (1 case). There was also a concentric narrowness of the visual field to red and green colors (2 cases). In 2 patients treated by amitriptyline there was an acute disorder of sight (a decrease in the acuity of sight, a narrowness of the visual field, etc.), related to a vascular spasm of the visual tract. The practical significance of complications brought on by antidepressive drugs is underlined. With early detection and treatment, all complications are reversible. All patients receiving psychotropic preparations should have a regular ophthalmological checkup. 6 references. (author abstract)

073900 Kaeser, H. E.; Scollo-Lavizzari, G. Neurologische Universitats-Klinik, CH-4051 Basel, Socinstr. 55, Switzerland /Acute cerebral disorders after high doses of oxyquinoline derivatives./ Akute zerebrale Storungen nach hohen Dosen eines Oxychinolinderivates. ***Deutsche Medizinische Wochenschrift (Stuttgart).*** **95(8):394-397, 1970.**

After the taking of about 30 tablets of Entero-Vioform (5-chloro-7iodo-8hydroxyquinoline) for diarrhea a 24-year-old man developed acute cerebral symptoms with confusional state, hallucination and precoma, followed by retrograde amnesia for 4 to 5 days. Two electroencephalogram leads demonstrated diffuse abnormalities which regressed rapidly, but bilateral focal changes in the frontotemporal region persisted. Similar abnormalities have been recorded in animals after oxyquinoline administration: it may lead to selective ganglion cell necrosis in the hippocanpus and the amygdaloid nucleus. 18 references. (journal abstract)

074566 Hes, J. Psychiatric Out-patient Clinic, Kupath Holim, Jerusalem, Israel On the use of Cath (Catha Edulis) among Yemenite Jews. ***In: Summaries Vol. 1: 3rd. International Congress of Social Psychiatry.*** **Zagreb, September 21-27, 1970. 247 p. (p. 42-43).**

The use, composition, and effects of the drug cathine, contained in the leaves of the plant, Catha Edulis, are described. Mastication of the leaves of Catha Edulis is very popular among

many inhabitants of East Africa and South Arabia. Yemenite Jews who immigrated to Israel brought this habit with them. Catha leaves contain 3 alkaloids: cathine, cathinine, and cathidine. Cathine produces euphoria, loquacity, and diminished feelings of hunger and sleep. The aftereffects are apathy, anorexia, and depression. The side effects consist of palpitations, sweating, thirst, drowsiness and dyspepsia. Mastication of Catha leaves is a social habit comparable with the drinking of tea and coffee or the smoking of cigarettes. However, psychic dependence is likely to occur and some cases of psychosis are reported. Psychosis due to Catha intoxication is characterized by incoherence, excitation, schizophreniform phenomena such as visual and acoustic hallucinations, and manifestations akin to delirium tremens. A remarkable phenomenon is the absence of physical dependence and the absence of tolerance to the drug. Catha intoxication, like amphetamine psychosis, usually subsides in a few days after stopping the intake of the leaves. (journal abstract modified)

074575 Jelic, V.; Momic-Muic, Z.; Kalousek, M. Department of Neurology and Psychiatry, Dr. M. Stojanovic General Hospital, Zagreb, Yugoslavia Our experience with toxic psychoses. *In: Summaries Vol. 1: 3rd. International Congress of Social Psychiatry.* Zagreb, September 21-27, 1970. 247 p. (p. 51).

Toxic psychoses resulting from the use of psychotropic drugs are discussed. The clinical picture of mental states produced by these drugs in some patients is like that of acute brain syndrome or deliriant states with confusion, restlessness, and fear. Most drugs, ranging from psychotropics to phenothiazine and antidepressants, including even antiparkinsonians, may promote the development of various psychoses, provided certain other conditions have been fulfilled. Thus, elderly patients, especially those with signs of some organic disease and manifest vegetative stigmata, have relatively often developed delirium after consumption of these preparations. It has further been noticed that a few days before withdrawal of these drugs deliriant disturbances disappear. Drug dosage, preparation and misuse are discussed and illustrated. (journal abstract modified)

075372 Fisher, W. J.; Akhtar, S. N. Nova Scotia Hospital, Dartmouth, N. S., Canada A case of bromism. *Canadian Psychiatric Association Journal (Ottawa).* 15(1):87-93, 1970.

The diagnosis of bromism depends upon: a high index of alertness on the part of the physician and the knowledge of the constituents of the brand name drugs he is prescribing, history of bromide ingestion over a long period of time, presence of mental symptoms with a bromide level of 150mgm (with the qualification that it may be lower if the drug were discontinued earlier), and an electroencephalogram (EEG) showing diffuse slow wave dysrhythmia. 3 references. (Author abstract)

075416 Edwards, H. Department of Psychological Medicine, The Welsh National School of Medicine, Whitchurch Hospital, Cardiff, Wales The significance of brain damage in persistent oral dyskinesia. *British Journal of Psychiatry (London).* 116:271-275, 1970.

The incidence of brain damage and buccal abnormalities was estimated in thirty four elderly chronic female patients with persistent oral dyskinesia and in a control group of thirty four patients matched for sex, age and phenothiazine intake. The incidence of brain damage was significantly greater in the dyskinetic group, but there was no significant difference in the incidence of buccal abnormalities. The significance of these results is discussed. 9 references. (Author abstract)

075417 Roxburgh, Peter A. Department of Psychiatry, Foothills Hospital, Calgary, Alberta, Canada Treatment of persistent phenothiazine-induced oral dyskinesia. *British Journal of Psychiatry (London).* 116:277-280, 1970.

A comparison of the features of persistent oral dyskinesia and functional oral movements is made. The literature on the drug control of oral dyskinesia is reviewed. In a double-blind interrupted cross over trial in two established cases of oral dyskinesia, thiopropazate dihydrochloride was found to be highly effective. 14 references. (Author abstract)

075472 Grounds, David; Davies, Brian; Mowbray, Robert. Melbourne, Victoria, Australia The contraceptive pill, side effects and personality: report of a controlled double blind trial. *British Journal of Psychiatry (London).* 116:169-172, 1970.

A double blind controlled trial of a contraceptive and an inert pill is described which studied the relationship between the side effects reported weekly to a general practitioner and questionnaire assessed neuroticism. Significantly more symptoms were complained of by women on the active

tablet and and these were less in the second month of the trial. No relationship was found between the presence of these symptoms and the degree of neuroticism in patients on the active tablet. 7 references. (Author abstract)

075839 Bloom, Joseph B.; Davis, Norman. Veterans' Administration Neuropsychiatric Hospital, Pittsburg, Pennsylvania 15206 Changes in liver disturbance associated with long-term tranquilizing medication (a follow-up study). *Diseases of the Nervous System.* 31(5):309-317, 1970.

A follow up study of changes in liver disturbance associated with long-term tranquilizing medication has been made. Case reports and histopathology are presented in addition to serum paper electrophoretic patterns for some patients. The results of rebiopsy of 11 or 20 original patients who showed liver histopathology reveals 3 to have worsened, 3 to show improvement and 5 to have remained the same. It is difficult to pin point the causative agent or agents producing these changes from the drug regimen of the patients. All the patients in this report still remain asymptomatic and anicteric. Periodic followup studies are desirable. 7 references. (Author abstract modified)

16 METHODS DEVELOPMENT

075427 Resnick, Richard B.; Fink, Max; Freedman, Alfred M. Department of Psychiatry, New York Medical College, 5 East 102nd STreet, New York, New York 10029 A cyclazocine typology in opiate dependence. *American Journal of Psychiatry.* 126(9):1256-1260, 1970.

A typological classification useful in the therapy of opiate dependence based on patients self ratings of their need for opiates is presented. Fourteen male subjects on cyclazocine treatment for up to 2× years reported less dependence on opiates for normal functioning than 17 male subjects who discontinued treatment. The existence of a consistent heterosexual relationship was significant in successful cyclazocine treatment. Enlisting patient's wives to supervise the daily cyclazocine intake has proven useful. 10 references. (Journal abstract modified)

17 MISCELLANEOUS

073734 Gershon, Samuel. The Neuropsychopharmacology Research Unit, Department of Psychiatry, New York University School of Medicine, New York, New York Lithium in mania. ***Clinical Pharmacology and Therapeutics.*** **11(2):168-187, 1970.**

The use of lithium in the treatment of acute mania and recurrent mania and the problems involved in making an evaluation of the data published are reviewed. Some of the problems of this evaluation are those of: differential diagnosis; rarity of manic depressive disease; cyclic disease patterns with a high incidence of spontaneous remissions; management problems associated with manic patients and their effect on design; prior and concomitant use of other psychoactive drugs; and lack of specific and relevant psychiatric rating devices for mania. It was found that a complete lack of controlled drug studies in mania with other established psychoactive drugs exists. No controlled studies have been undertaken to determine the prophylactic activity of lithium or any other psychoactive drug for recurrent mania. No valid conclusions can be reached from the data available on lithium and mania. 84 references.

073787 Mashkovskyy, M. D. Vsesoyuznyy Nauchno-issledovatel'skiy Khimiko-farmatseuticheskiy institut imeni S. Ordzhonikidze, Moscow, U.S.S.R. /The adrenergical mechanisms of action in antidepressive drugs./ Adrenegicheskiye mekhanizmy deystviya antidepressantov. ***Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva).*** **70(5):751-759, 1970.**

The author gives concise information on the influence of psychotropic preparations on the adrenergical processes in the CNS. The significance of the adrenergical processes in the pathogenesis of depression and the mechanism of action of contemporary antidepressive drugs is stressed. Methods of pharmacological studies, used in the search of new antidepressive drugs are considered. 90 references. (author abstract)

074217 DiMascio, Alberto; Demirgian, Edward. Boston State Hospital, 591 Morton Street, Boston, Mass. 12124 Antiparkinson drug overuse. ***Psychosomatics.*** **11(6):596-601, 1970.**

Evidence is presented which indicates that antiparkinson drugs are being overused. Two commonly held practices were considered and found unwarranted: the prophylactic prescription for antiparkinson drugs, and their extended prescription for the term of pharmacotherapy. At the moment, on the basis of the best evidence available, antiparkinson drugs should be prescribed only after extrapyramidal side effects occur, and usually only for a period not to exceed 3 months. 14 references. (Author abstract modified)

075420 Brodsky, Carroll M. University of California Medical School, San Francisco Medical Center, San Francisco, California The pharmacotherapy system. ***Psychosomatics.*** **11(1):24-30, 1970.**

The analysis of the pharmacotherapy system presented here is based on data about pharmacotherapy practices gathered from inpatient and outpatient services and from experiences in teaching students, residents, and other physicians about the uses of drugs. In the decision making process about psychoactive drugs, the physician is influenced by many factors including, besides the needs of the patient, the patients's family and time considerations. Study of the pharmacotherapy system by systems research methods is recommended, also that if pharmacotherapy must be studied as a system it can only be taught as such. 13 references. (Author abstract modified)